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Chemotherapy

Dramatic progress in many directions continues to be made in the applications of chemistry and biochemistry to the eradication of disease. We hope in due course to publish authoritative articles dealing with many of these topics in detail. A definition of the scope of true chemotherapy is hard to frame, and the progress of research may soon pass the boundaries of artificial limitation. We may assume, however, that the term implies the cure of infections caused by micro-organisms with the aid of substances of known or partly known constitution.

The father of the subject was Paul Ehrlich, who noted in 1891 that the malarial parasite is stained by methylene blue; he then tried to find dyes and, later, what may be called colourless dyes, which would kill the micro-organisms without damage to the host. Methylene blue itself was found to have some action against quartan malaria. Perhaps the first notable result was the discovery of trypan red (1904), which cured an otherwise mortal infection of mice by trypanosomes. The organic arsenicals, atoxyl (Thomas, 1905), salvarsan, neo-salvarsan, tryparsamide, etc., are milestones along the road opened up by Ehrlich, and some of them are still essential to the physician. Analogously, organic antimonials have been introduced into medicine, and in retrospect we cannot ignore the mercurial treatment of syphilis, sometimes attributed to Paracelsus.

The appearance of Bayer 205 for the treatment of sleeping sickness was probably the direct result of Ehrlich's work; it was a great step forward because this complex derivative of benzene and naphthalene contains no arsenic or similar toxic element. In the last few years King, Ewins, and Warrington Yorke have shown that certain aromatic diamidines are highly effective against various protozoa.

We can make only a brief reference to the highly important subject of the chemotherapy of malaria. Quinine retains its position in the treatment of acute infections, and though many active analogues of the alkaloid are known, none has been introduced into practice. The more successful synthetic antimalarials appear to have been developed by following up Ehrlich's observation with methylene blue. They are plasmoquine (1926), a quinoline derivative, which is said to destroy the sexual form of the parasite (crescent or gamete), and atebrin (1932), an acridine derivative, which like quinine attacks the asexual form (schizonts). We owe these resources to the outstanding work of Roehl and Schulemann and their colleagues. Many similar drugs have been recommended and the present time is one of intensive research, due in part to the occupation of the Dutch East Indies by the Japanese.

The guiding hypothesis in this period was the idea of direct action on the micro-organism. Ehrlich imagined that the cells of the organism to be attacked contained various receptor groups of protein or enzyme molecules, and considered his problem to be the recognition of these groups and the elaboration of suitable toxic substances to combine with them.

For a long time there was no chemotherapy of bacterial infections, although the possibility was recognized after it had been shown that acriflavine or proflavine need not kill trout ova which they nevertheless sterilize (Blake), and after Morgenroth and Levy cured mice, experimentally infected with pneumococci, by means of ethyldihydrocupreine. These observations were of no practical importance (except for local infections), and the discovery of prontosil by Domagk brought about a revolution, not only in treatment but also in the attitude of biologists to the study of chemotherapy.

Prontosil is an azo-dye, and very soon Tréfouel and others found that one of its components,

sulphanilamide, is alone responsible for its activity. Sulphanilamide is relatively non-toxic to man and is used in massive doses against virile strains of haemolytic streptococci. It has reduced the mortality of puerperal fever to an amazing extent. The drug is also of value in keeping wounds clean, provided that the greater part of the infective material has been removed.

Sulphanilamide is not effective against meningococci, gonococci, and pneumococci, but certain derivatives such as sulphanilylaminopyridine (M. and B. 693, Ewins and Phillips), sulphathiazole, and sulphadiazine are now among the physician's sheet-anchors in the treatment of meningitis, gonorrhoea and pneumonia. The cures brought about are often as magical as those of scurvy by vitamin C. Sulphanilylguanidine is claimed as a remedy for bacillary dysentery, and the sodium salt of acetylsulphanilamide is useful in combating certain infections of the eye. There is already an enormous literature of the sulphanilamides, but we may be sure that still better compounds of the series will eventually be found. It is even probable that a supply of the perfected drug will be kept in most households and will be taken when the need arises with as little compunction as an aspirin tablet. Sulphamethazine, recently introduced by British chemists, approaches this ideal on account of its low toxicity, and the results of further chemical trials will be scrutinized with great interest.

Several workers obtained extracts which antagonized sulphanilamide, and finally Woods (1940) showed that *p*-aminobenzoic acid counteracted the action of the drug. According to Fildes, who has extensively studied bacterial growth factors and growth inhibition factors, aminobenzoic acid is an essential metabolite, and sulphanilamide is bacteriostatic because it interferes with the normal growth-promoting action of this metabolite. Fildes has emphasized that here we must have the rational approach to research in chemotherapy, and the idea is being enthusiastically followed up by numerous investigators. For example, McIlwain has very recently shown that analogues of pantothenic acid possess bacteriostatic action in certain cases. Roughly the idea is that of the cuckoo in the nest, and it helps us to understand why the dosage of some of the newer remedies must be so high. A kind of mass action replacement of a normal essential for growth is involved.

Surely this would suffice for a few years' progress, but the story continues. In 1929 Fleming found that suitably grown *Penicillium notatum* produced an anti-bacterial substance, termed penicillin, which differed in important particulars from the sulphanilamides. Its action, though bacteriostatic rather than antiseptic, is not interfered with by bacterial extracts, pus fluids, or *p*-aminobenzoic acid. Florey and others showed how to prepare penicillin for therapeutic use and demonstrated its value clinically. The chemical constitution of this important substance has not yet been elucidated, but it is already certain that it is effective in very high dilution, that it is almost completely non-toxic, and that, unlike the sulphanilamides, it may be used against staphylococci. Somewhat similar properties, except in respect of toxicity, are claimed for gramicidin, which has been isolated from soil. It is a polypeptide containing tryptophan units.

The outstanding problems among bacterial infections are tuberculosis, typhoid, and cholera, and in each case there are indications that may be followed. The end is not in sight, but we are marching along a road that will lead to it. Witnessing the dawn of a day of hope we may be comforted by the reflection that these tragic years are making some amends by contributing to the alleviation of the sufferings of humanity. Chemotherapy is a benevolent legacy to posterity that will gather compound interest.

Contributions and correspondence should be sent to the editor: E. J. Holmyard, M.A., M.Sc., D.Litt., F.I.C., Imperial Chemical Industries, Nobel House, Buckingham Gate, London, S.W.1. Scientists engaged in research of an interesting or important character are invited to send short notes on work in progress and results obtained.

Metals

SIR LAWRENCE BRAGG

We associate metals with hardness, toughness, and strength. But a curious paradox lies at the root of the valuable mechanical properties of the metallic state: in order to be strong, a metal must be weak. This paradox, and the equally surprising fact that, in a sense, metals are not true solids at all, are among the topics here discussed by Sir Lawrence Bragg.

(1) WHAT METALS MEAN TO US

We employ various materials to build or fabricate the many objects we use in everyday life, choosing those whose properties are most suitable for the purpose which the object has to serve. Certain of these materials have been used from the earliest times, such as stone, wood, leather, and animal or vegetable fibres, each with its own peculiar valuable properties. Stone resists crushing and is very durable and permanent, as indeed it must be, since it has so long resisted change as a part of the earth's crust. It is therefore ideal for walls and buildings, and very early in his history man discovered how to make artificial stones by burning clay, with the advantage that they could be given any desired shape, and made into bricks or given elaborate forms as pottery. Wood is strong and tough and light, it resists tension as well as compression, and is not brittle like stone. It forms beams and furniture and parts of tools or weapons. Leather is tough but at the same time it is flexible; it is ideal as straps or sheets. Vegetable fibres such as linen or cotton, and animal fibres such as wool and silk, owe their value to their flexibility and strength in resisting extension. They can be spun into yarn or rope, and woven into cloth. The technological age in which we are now living is replacing the natural products used by early man by a series of artificial products, but it is remarkable to see how in nearly every case we are copying Nature's materials. The wide use of concrete represents a developed art of making artificial stone. Artificial fibres such as rayon or nylon replace cotton, wool, and flax. Plastics are coming very much to the fore; they correspond to early man's use of horn, another substance with peculiar properties of toughness in all directions without the 'grain' of wood. For the most part we are following in the footsteps of our remote ancestors, though we can make for ourselves what they had to cull from wood and field. There are exceptions; for instance, we have discovered comparatively recently the number of uses to which natural rubber can be put, and are now making it artificially. This is a really new discovery; our ancestors had nothing with such remarkable powers of elastic stretching without breaking, and resistance to being abraded.

Metals represent one vast range of materials, however, which have no natural counterpart. They have to be won from the earth, where they exist in a cunningly hidden form. Mankind only slowly realized their potentialities. They were at first rare and precious, used for very special purposes. Great store was set by them, and trade routes sprang up for their commerce. It must have been by chance that some early Tubal-cain discovered that when certain stones were heated in the fire, a substance with hitherto undreamed of properties could be beaten out, and so became, as Genesis relates, 'an instructer of every artificer in brass and iron.' Modern civilization is based upon the use of metals to an extent which is always increasing at a truly extraordinary rate. Sir Thomas Holland, in reviewing our resources, states that far more metal has been taken from the earth by men since 1900 than in the whole of the previous history of mankind.

What gives metals this distinctive character we all recognize as 'metallic,' which makes them play a quite unique part in our material civilization?

Their most striking mechanical attribute is that they are hard and strong in resisting compression and extension, and that at the same time they are tough and can be distorted without breaking. They can be dented or hammered or drawn into wire, and so far from being weakened by maltreatment of this kind, they become even stronger than before. A stone is hard and strong, but once it yields it breaks completely; it is brittle. What new possibilities were opened up to primitive man when, instead of flint, he first came to know of a material for weapons and tools which was as hard as stone and yet could be relied on not to snap!

Again, metals can be moulded to our purposes by heat. Familiarity dulls the keen edge of appreciation, but most of us can probably remember the thrill of seeing a blacksmith make a horseshoe, converting the strong iron into something as soft and pliable as clay by heating it red-hot. The final properties of steel depend on the history of its heat-treatment. A steel spring, if heated and cooled slowly, is relatively soft and can be bent into any desired shape, cut, or drilled. If it is heated and suddenly cooled or 'quenched' it becomes very brittle. Warm it up again to a relatively low temperature, and it becomes 'springy.' Or take the kind of iron from which files are made, containing a high proportion of carbon. If cooled slowly it is so soft that the teeth of the file can be cut on it. Heat it, and quench it by plunging it into brine, and it becomes glass-hard and fit for its work. It is such properties which make metals the ideal materials for the vast complex of machinery on which we now depend.

Metals are essential to us in another way now that we have made electricity our servant. They conduct electricity, and iron (along with some other elements) can be magnetized. A cable is laid across the Atlantic; in other words a few strands of copper wire are surrounded by a thin sheath of rubber composition and deposited on the sea floor. What a remarkable thing it is that if an electric current is fed into the cable in England, it prefers to travel along the wire to America rather than jump the intervening inch or so of insulator which is all that prevents it taking a short cut back home through the sea! I think it was Oliver Wendell Holmes who, on seeing a tram drawing its energy from a tenuous overhead wire, said it was power stripped stark naked. The possibility of sending messages and power by a metallic conductor has had incalculable social consequences. It has linked the world into an organic whole by providing it with a system of nerves by which the consequences of what happens in one part of the globe are immediately felt in other parts. Biologists rank living things in a scale of ascending complexity of their nervous systems; we are living in a world which has possibilities of much higher organized life than that of our forefathers, and we are trying to adjust ourselves to the new conditions, with shattering consequences. The use of metals has brought about the change. The present war is fought with weapons of metal made by metal machines; the possession of sources of metal determines its strategy; the whole world has been involved in it because of the metallic links which bind it together. One may say that the vastly increased use of metal has determined the character of the war, and to a large extent has been responsible for the social changes which have brought it upon us.

(2) THE METALLIC STATE

The science of chemistry is concerned with the compounds which are formed when the various elements are combined together. The atomic theory had its origin as an attempt by Dalton to explain the proportions in which the elements combine. More recently, physicists have studied the structure of the atom, and have gained a greater understanding of the forces which bind atoms together. It would take us too far to plunge into the theory of atomic structure in this article, but certain aspects of it may be recalled which indicate the fundamental nature of the metallic state.

The many different kinds of atom, some ninety odd in all, may be roughly divided into two great classes, electropositive and electronegative. The periodic table displays the elements ranged in ascending order of atomic complexity, and in it the inert gases which have no chemical affinities stand out as neutral landmarks at important points in the table. The atoms which occur after them in the table are markedly electropositive, those which come just before are equally markedly electronegative, and the character changes as one passes from one inert gas to the next in the series. Interpreted in terms of atomic structure, the electropositive atoms are those which easily part with one or more of the negative electrons surrounding the nucleus of the atoms, and thus change from neutral atoms into positively charged ions. The electro-negative atoms easily absorb one or more additional electrons into their structures, changing from neutral to negative in charge. These two classes are the Bulls and Bears of the atomic Stock Exchange; the one has electrons it is prepared to sell, the other lacks electrons and is willing to buy. The majority of elements are electropositive; they are the metallic elements.

To continue our broad generalization, which we will not confuse by the qualifications which would have to find a place in a more detailed account, there are three main types of compound, or association of atoms. They are illustrated in a pictorial way in figure 1.

The most simple is an association of electropositive and electronegative atoms. Common salt, NaCl, is an example. The electropositive

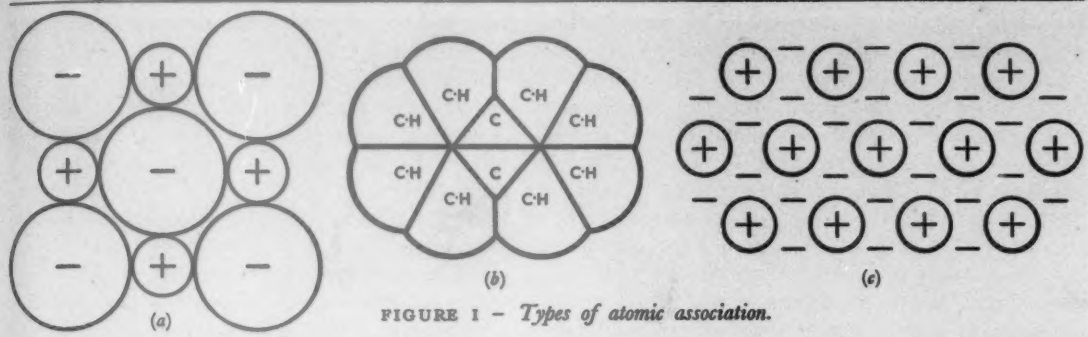


FIGURE 1 – *Types of atomic association.*

atoms of the metal sodium part with their electrons to the electronegative atoms of chlorine. The resulting positive sodium ions and negative chlorine ions are held together by electrostatic attraction, as in figure 1 (*a*), in a kind of chessboard pattern. Such a structure is typical of inorganic salts in general, although the negative unit is often a complex of several atoms.

Quite a different type of association is characteristic of organic compounds. Two or more electronegative atoms, both short of electrons, fuse their structures into an intimate combination. This tightly knitted whole, like that of naphthalene illustrated in figure 1 (*b*), is what the chemists term a 'molecule.' Such a molecule can go through physical adventures, such as melting, vaporizing, or being dissolved in a solvent, while still remaining an entity. The electronegative elements carbon, oxygen, and nitrogen have the strongest powers of forming such groups, and with a ballast of hydrogen they form the basis of the vast complex of compounds studied by the organic chemist.

In fibres, such molecules are incorporated in long chains by linking each to the next. In horn, and in some plastics, they are joined by side-links as well. Long chains with links free to rotate, so that they can wriggle, and joined only by infrequent side-bands, form a material with the properties of rubber. It can be seen that this power of linking on any number of atoms to the structure leads to an infinite variety of molecular forms. Nature has seized upon this possibility in order to construct the vast molecules of which living bodies are built, containing thousands of atoms, where the complexity is necessary to enable them to perform such varied functions.

The above may be called the plus-minus and minus-minus chemical compounds; there remains a third class, the plus plus, shown in figure 1 (*c*). It is composed of atoms all of which lose electrons easily. We may think of it as an array of positive ions, with a system of electrons held in common between them all. It is quite a different type of compound from those illustrated by (*a*) and (*b*). The relative numbers of atoms in (*a*) are fixed by the alternation of plus and minus, and in (*b*) by their association into definite family parties or molecules. In (*c*) it is possible to replace one kind of electropositive atom by another, as long as the newcomer is not too incompatible in size and other properties with its neighbours. When the atoms are all of one kind we call the structure a pure metal; when they are mixed we call it an alloy, and it is natural to find that the electropositive or metal atoms can be alloyed together in a wide range of proportions. The general cloud of electrons can drift through the structure, endowing the metal with its power of conducting electricity.

(3) A MODEL WHICH ILLUSTRATES THE METALLIC STRUCTURE

We have seen that the metallic state has certain peculiar features. In a sense metals are not true solids. There are no direct bonds between atom and atom binding the whole together. The positive ions actually repel each other, and are only held in a compact mass by the attraction of the negatively charged common system of electrons. This structure indicates the explanation of the most characteristic feature of a metal, the way in which it can be hammered or dented or rolled without breaking down its continuity. However the atoms slither over each other, the continuous electron cloud remains to hold all together. A metal is more like a crystallized liquid than a solid.

An immediate reaction to such a picture of a metal is the question why a metal has any strength at all if the atoms can slide over and past each other so easily. The answer is very interesting. If a pure metal is cooled from the molten state under controlled conditions so that the atoms are

built into a single perfect crystal, it has practically no strength at all. Professor Andrade wrote an article for the April 1942 number of ENDEAVOUR in which he described experiments on the slip of metal single crystals. It is a queer experience to handle such a crystal in the form of a long rod. It is as weak as a similar rod of plasticine and can be stretched at first by the fingers with hardly any resistance. Directly it is distorted by stretching, however, it becomes stronger, and finally when it is thoroughly maltreated it assumes the strong rigid character we associate with metal in the ordinary state. A simple experiment with a copper wire illustrates this feature well. If the wire is supported horizontally by one end and a Bunsen flame played along it, the wire becomes very soft. It does not become a single crystal, but it 'anneals' into a conglomeration of highly perfect crystals which show the effect. In this state, a very small weight hung on its end bends it over. Bend it back to the horizontal position, and it will support the weight. Bend it backwards and forwards a few times, and it becomes very stiff. 'Cold work' has made it strong.

A two-dimensional model of the metal structure can easily be made which illustrates these properties in rather a fascinating and suggestive way. Our model must have numerous 'atoms' of exactly equal size; these atoms must be round, they must slither over each other without any friction, and there must be some general force of attraction holding the whole together. Figure 2 shows a raft of tiny bubbles floating on the surface of a soap solution, which will do just what we want. The little bubbles all stick together by capillary forces, like the 'sixpence' in one's teacup when it is stirred. By blowing them through a small orifice under the surface with a constant pressure equal to about 20 cm. head of water, a remarkable constancy of size can be achieved. The perfection of the rows in the 'crystal' of figure 2 is evidence of the regularity. The bubbles are about 1 mm. in diameter.

A raft roughly rectangular in outline can be attached to supports on either side, and we can try the experiment of shearing it. Springs just lying on the surface of the solution make convenient supports because, by adjusting the tension, one can make the pitch of the spring fit a row of bubbles on either side. If now one spring is slowly moved tangentially, the raft at first strains elastically. After a certain amount of sheer strain, however, one can see a few bubbles on one of the free edges becoming unstable and slithering over each other, and then suddenly a movement runs along a row from one edge to the other across the raft like a ladder in a stocking. The bubbles in turn 'move on one,' and when this movement has gone right across, the top and bottom of the raft become displaced by one bubble width relatively to each other. This can be repeated several times. Figure 3 shows typical rafts—(*a*) before and (*b*) after a succession of these movements of slip. When a single metal crystal is extended, as Professor Andrade has found, it does so by slipping along crystal planes as shown in the beautiful illustrations of his ENDEAVOUR article; in our two-dimensional model we have 'slip-rows' which behave in a similar way.

The graph in figure 4 shows how this phenomenon may be studied quantitatively. The ends of one of the springs are attached to a pair of long thin vertical glass fibres which are held rigidly at their far ends. A telemicroscope with a scale in its eyepiece is focused on one of these glass fibres, so that we can measure the force on this spring by watching the displacement of the fibre. The other spring is moved parallel to itself by a micrometer head. It is thus possible to establish a stress-strain curve as shown in figure 4, where the strain or relative movement is plotted horizontally and the stress measured by the bending of the glass fibre is plotted vertically. The upper graph runs from left to right. The raft is at first elastic as shown by the upward slope of the graph, until the point is reached where slip takes place, when the stress falls back to zero or even a little past the zero. As we continue to shear, it builds up again till further slip takes place. At the end of the upper graph the shearing movement was reversed, and the graph repeated in an inverted form.

In the next paragraph I wish to indicate the significance of this effect as regards the strength of a metal, but before leaving our model I would like to draw attention to some other suggestive features. In a single perfect crystal the atoms are arranged in absolutely regular rows and sheets.

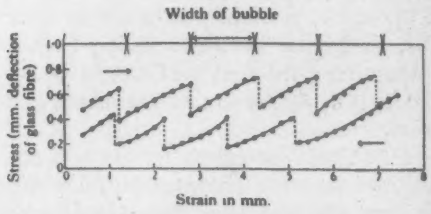


FIGURE 4 – *A stress-strain curve for the sheared raft. It yields each time the shearing movement increases by one bubble width.*

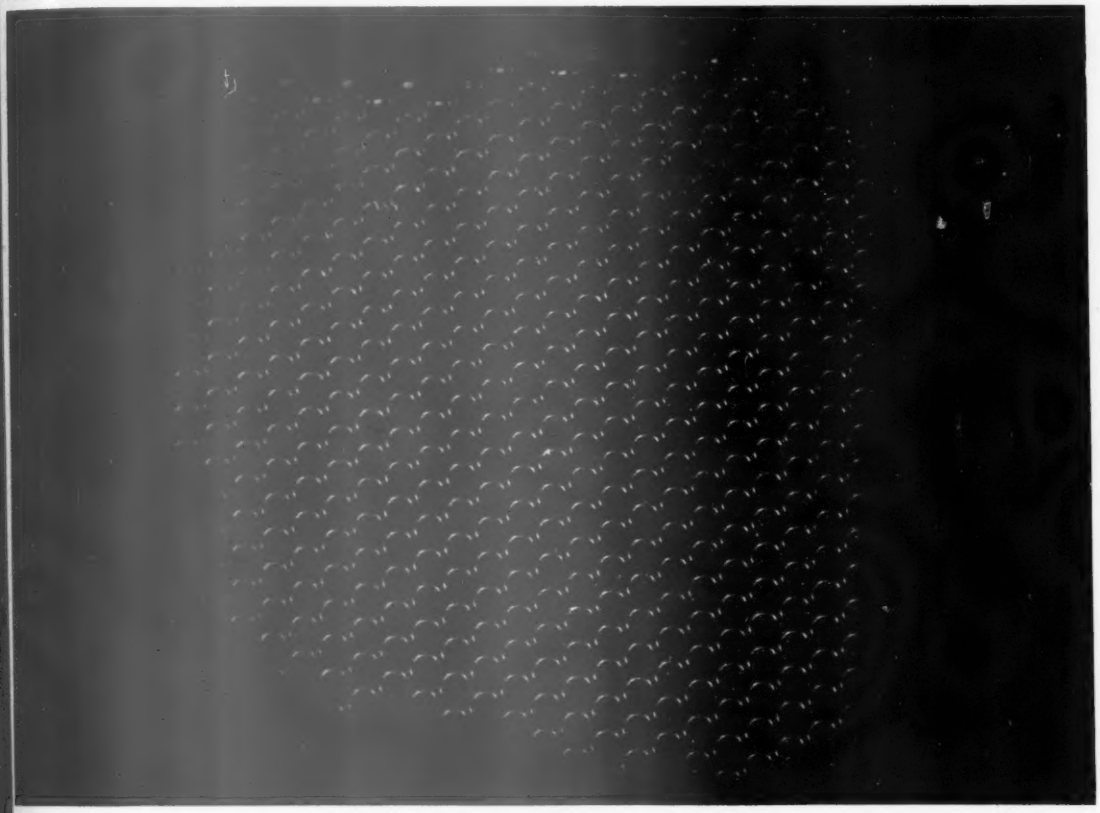
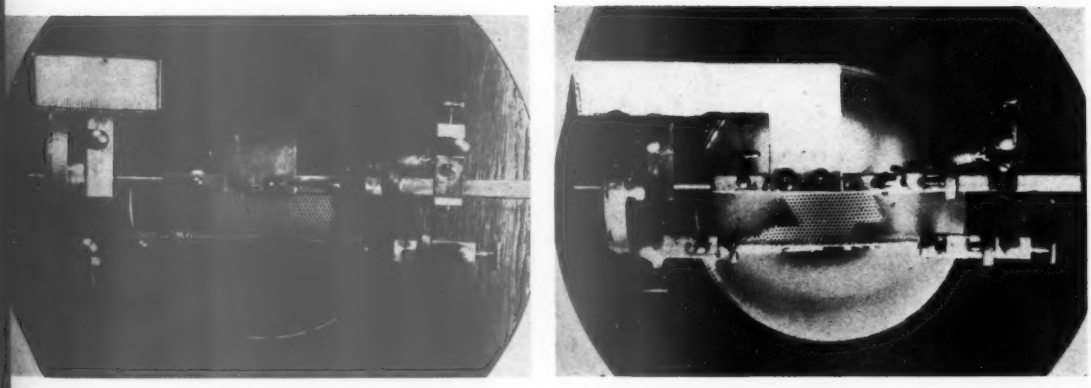


FIGURE 2 – *A perfectly crystallized raft of bubbles.*



(*a*) (*b*)

FIGURE 3 – *Rafts before and after a succession of 'slip' movements.*

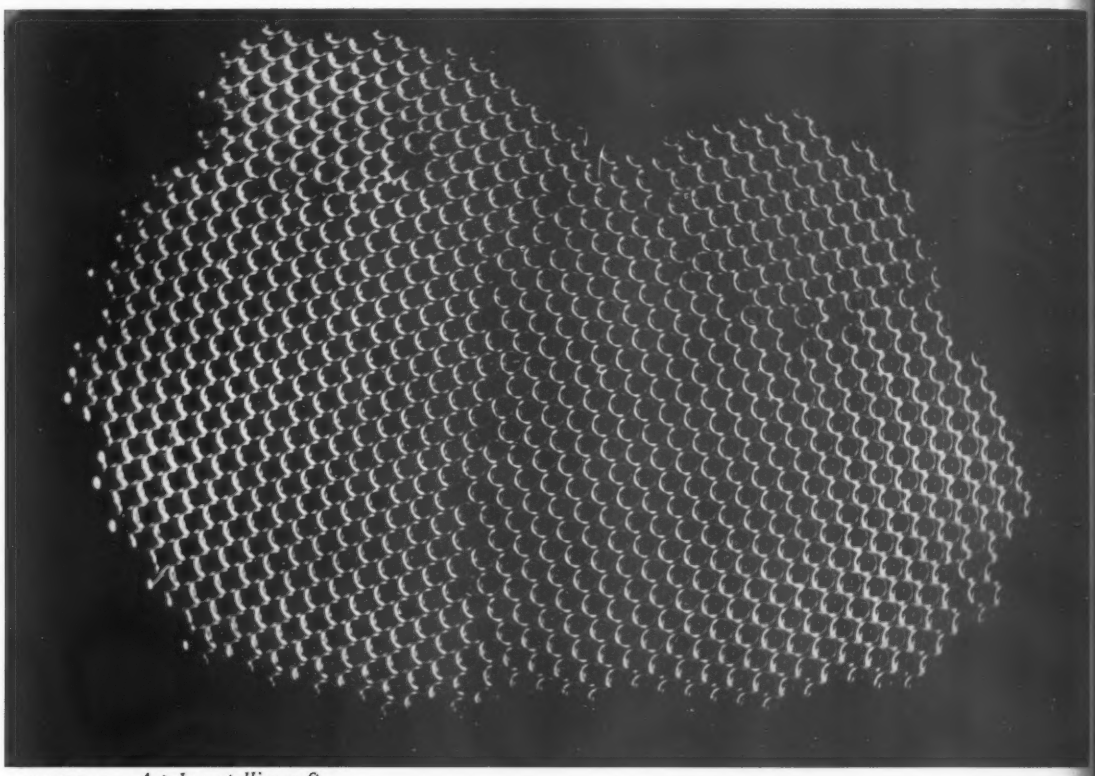


FIGURE 5 – *A polycrystalline raft.*

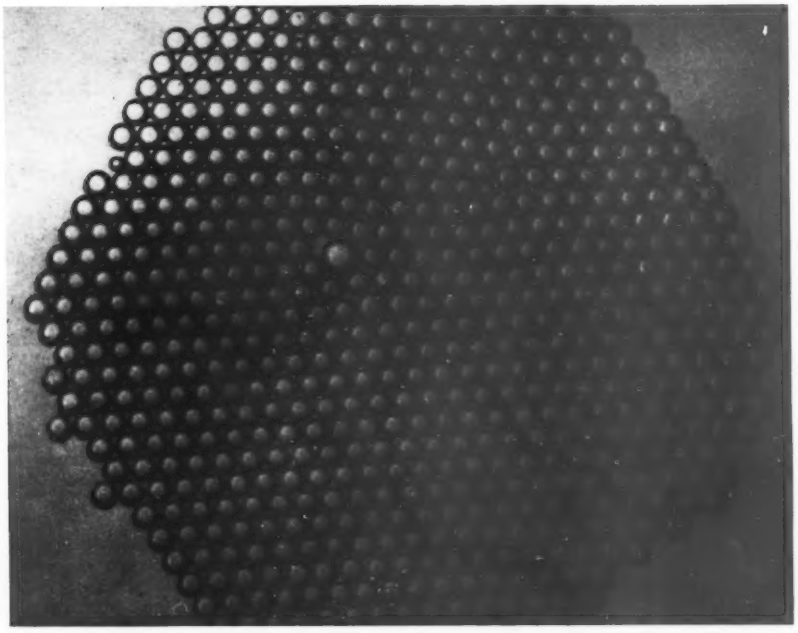


FIGURE 6 – *The effect of a foreign atom.*

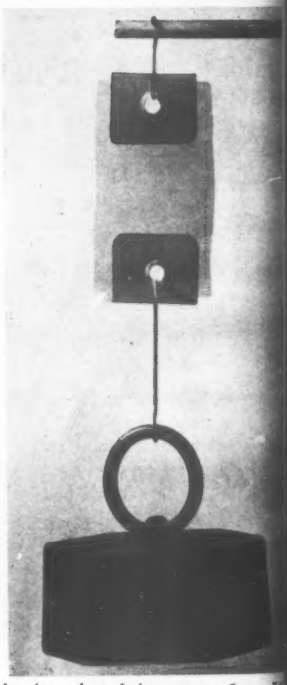


FIGURE 9 (*right*) – *A strip of* 'Cellophane' 10 × 5 × 0·002 *cm. supporting a* 2 *kg. weight, its edges being stress-free. If touched by a needle-point, it breaks instantly when dry, but is unaffected when moist.*

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ss-free. If

When, however, there are a number of crystals in the metal which are variously orientated with respect to each other, the atoms at the boundaries must somehow adjust themselves so as to make the best of both worlds. Figure 5 shows a raft composed of four such 'crystals,' and it is interesting to see the way the boundary is marked out by a series of dislocations or misfits. The structure of each crystal can be seen right up to the boundary, but it is slightly distorted by the necessary adjustment of the atomic positions at the boundaries. We can see that a simple slip process is confined to one crystal only; it cannot continue into the next, when a fresh start must be made. Figure 6 illustrates another feature which is exceedingly important in metallic structure. A few bubbles of different size have been deliberately introduced to represent atoms of impurity in the metal. They spoil the regular structure in a remarkable way, upsetting the rows for a considerable distance. We see here an explanation of the very large influence of small amounts of impurity on the mechanical and other properties of a metal. Each atom of impurity affects a large volume all round it because it throws the regular rows out of their stride.

Another feature well shown by the model is the power of the metallic structure to recover from distortion. It has an indestructible crystallizing power: it cannot stay in an amorphous or irregular condition. The raft can be crushed by moving one spring towards the other. Slips take place along rows in directions making 120° with each other, but the bubbles always adjust themselves so that the raft remains crystalline. By moving the springs slowly apart again, we can 'draw out' the raft, and again the bubbles slip and move so that new rows appear between the springs and we are left with a regular crystal as before.

(4) THE STRENGTH OF A METAL

A single perfect crystal of a metal is extremely weak, gliding along its slip planes with hardly any resistance. If, however, it is cold-worked, the perfection of the structure is destroyed. Different parts are orientated differently, and many dislocations like those illustrated by figure 5 must be created. At the same time it becomes stronger, so the strength must in some way be dependent upon the distortion of the structure. We can use the analogy of the model to show how this comes about, and even to calculate in a rough way an estimate of its strength which is in approximate accord with that measured experimentally.

Figure 7 shows typical measurements of stress and strain made with a test piece of polycrystalline pure iron by Smith and Wood. As the tension is applied to the specimen, at first it yields elastically as shown by the lower curve, and if the tension is released it recovers its original length. Beyond a certain point, about 8 tons to the square inch in this case, it yields. It is pulled out by the tension, and does not recover if the tension is released. The yield is very large compared with the elastic extension, so the strains for the upper curve showing the yield are plotted on a scale reduced a hundredfold. In yielding, it is distorted and hardens, so being enabled to withstand the greater strain, until finally at about 18 tons to the square inch it breaks. The yield-point, as we have seen, is greatly influenced by the previous history of the metal. Yield occurs at a low stress if the metal is well annealed and at a high stress if it has previously been cold-worked. The coefficient of elasticity, which defines the ratio of stress to strain, is, on the other hand, almost independent of the state of the metal, and is only slightly affected by impurities. In other words, all samples of iron follow at first the same curve in figure 7 within their elastic range, but may break away from it at very different points. This distinction is important. To define stress and strain, we may picture a cube of the material of unit dimensions on each edge. The shear stress is the tangential force on opposite faces tending to slant it over, the shear strain is the angle it is slanted through in consequence. The coefficient of elasticity is the ratio of stress to strain.

A possible clue to the factors which determine

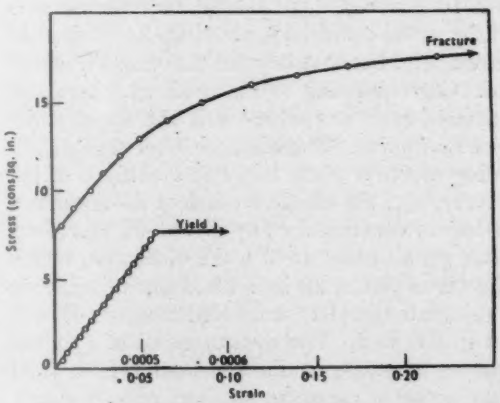


FIGURE 7 – *The stress-strain curve for pure iron.* (*S. L. Smith and W. A. Wood*, Proc. Roy. Soc., *May* 1941.)

the point at which a metal ceases to stretch elastically, and begins to yield, is afforded by figure 4. The little raft of bubbles shears elastically until its top edge has moved on by about one bubble width as compared with the bottom edge; the stress is then released by a slip of one row of bubbles over the other. It must obviously wait until it is sheared about this amount before it is worth while slipping, so to speak, because if it slipped when it had only moved on a fraction of a bubble width it would end up with a greater strain in the opposite direction. If s is the width of a bubble and t the breadth of the raft, the shear strain builds up to an amount about s/t before slip takes place.

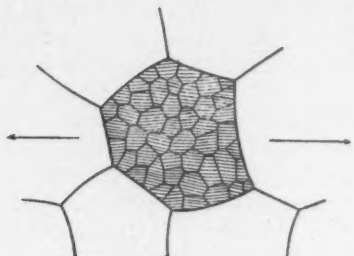


FIGURE 8 – *A diagrammatic representation of the fragmentation of a metal crystal by cold work.* (Nature, 1942, **149**, 511.)

Now picture our metal as built up of a number of differently orientated units as in figure 8, of average size t. Each bit must slip independently, and the smallest jump which can take place is the distance s between nearest atoms, like the bubble width in figure 4. We should therefore expect that the metal could be strained up to an amount s/t elastically, but that beyond that point it would yield. Corresponding to the *strain* s/t, there will be a yield *stress* ns/t where n is the appropriate elastic coefficient. The distance s between neighbouring atoms is given by crystal analysis of the structure, and the elastic coefficient for shear is a well-known constant for any metal. If, therefore, we can get an estimate of t, the dimension which limits the extent of an individual slip process, we can calculate the yield stress and compare it with what is observed. The measurement of t should of course be made on the specimen whose yield we are going to measure, because, once it yields, t gets smaller and the yield-point goes up.

We can make a shot at the elusive t by means of a well-known optical principle. A highly perfect optical grating with a large number of regularly ruled lines produces very narrow or 'sharp' spectra when monochromatic light is diffracted by it. If the number of lines in the grating is reduced, the spectra become broad and diffuse, and there is a simple relationship between the number of lines and the breadth of the spectra. A corresponding phenomenon is observed with X-rays. The X-ray diffraction lines produced by a well-annealed specimen of pure metal are sharp, but when the same metal is cold-worked the X-ray lines become broad and fuzzy, owing to the breakdown of the perfect crystals and the creation of dislocations and strains. There is a limit to the amount the lines can be broadened in this way. The metal has a high power of recrystallization, and if momentarily excessively shattered it heals its wounds to a certain extent. Wood has estimated the lower limit of fragment size in several pure metals by ascribing the whole of the line-broadening to size effect, and in the following table these breadths are used to calculate their yield stresses in shear:

	s (cm.)	t (cm.)	ns/t (tons/in.^{2})
Copper ..	$2{\cdot}56 \times 10^{-8}$	$0{\cdot}7 \times 10^{-5}$	10·6
Nickel ..	$2{\cdot}49 \times 10^{-8}$	$1{\cdot}2 \times 10^{-5}$	10·3
Silver ..	$2{\cdot}88 \times 10^{-8}$	$0{\cdot}8 \times 10^{-5}$	6·7
Iron[1] ..	$2{\cdot}42 \times 10^{-8}$	$3{\cdot}2 \times 10^{-5}$	4·1

It is interesting to see that these calculations give figures of about the right amount. When one goes into the matter more closely, however, many complications appear which show that we are touching only the fringe of the problem. Different X-ray diffraction lines in a given specimen do not broaden to the same extent, as if, to put it loosely, the perfection had a different range along and across the grain. The form of the distortions in the metal is unknown, for it will be seen from the above table that they are on far too small a scale to be measured under the microscope. There is the serious objection to the above calculation, that the broadening is probably largely due to local strains in the metal caused by the cold work. Such strains cause variations in the scale of the crystal pattern from point to point, and so also make the diffracted beams diffuse. Nevertheless, it is interesting to note that if we assume that, by estimating the range of perfection by the breadth of the X-ray lines, we are also estimating the

[1]This figure is for pure iron, which is a very weak metal as compared with the carbon-containing iron to which we are accustomed.

dimensions of the individual slips, we do get figures which are at any rate of the right magnitude.

We can now see in a qualitative way why a metal is strong, and how its strength can be increased. It is strong if each little slip process is confined to a short run in the metal and not allowed to spread over large perfect crystal grains. This restriction can be brought about by cold work and by putting foreign atoms in the metal to spoil its perfection of structure. Figure 6 illustrates the effect of atoms of impurity which distort the regular rows.

One might now ask, why not spoil the structure so much as to inhibit slip altogether, and so make it exceedingly strong? Here we come up against a curious paradox, which is really at the root of the valuable mechanical properties of the metallic state. *In order to be strong, a metal must be weak.* A body which cannot slip is brittle. When it is pulled, there is bound to be somewhere a minute crack or point of weakness, as was first pointed out by Griffiths, and at the sharp end of this crack there is an excessive strain which causes the crack to deepen; in other words, the material tears across. Brittle substances can be strong in compression because cracks do not then extend, but they will not stand being pulled. In a metal, on the other hand, just because it yields when it is pulled too hard, a crack will not deepen. The metal gives way at this point and relieves the strain. A very simple experiment which anyone can try illustrates this effect. The 'Cellophane' used for wrappings is brittle when dry, slightly plastic when moist. By gumming cardboard supports to the top and bottom of a strip of 'Cellophane,' leaving the edges free as in figure 9, so that cracks do not start from them, one can hang on it a very considerable weight. If it is pricked with a needle-point when dry it breaks instantly. If now one breathes on the 'Cellophane,' the needle-prick has no effect. The 'Cellophane' flows enough around the pricked point to stop the spreading of a crack. I am obliged to Dr Orowan for this illustration[1].

Here is another one of a more homely character. A smile is ordinarily quite a pleasant movement, but we all know how painful it can be when the strain is concentrated at one point due to the rigidity associated with a cracked lip.

[1]Note that for this experiment to succeed when the air is moist the 'Cellophane' sheet must first be artificially dried.

(5) SUMMARY

At the beginning of this article, the peculiar metallic attribute which makes metals an essential basis for tools, machines, and structures was defined as a combination of strength and rigidity with toughness. We can now see how this peculiar combination of opposed qualities is brought about. The metal parts of a machine may give elastically, but they must not yield in the sense of becoming permanently deformed by the strains ordinarily placed upon them. Yet they must always hold this power of yielding in reserve, so to speak, if the metal is to retain its other precious property of reliability. As Griffiths has shown, thin fibres of glass or silica can be as strong as steel if they are fresh and have no cracks, but a touch on their surfaces makes them snap instantly under a strain. Though glass is harder than steel we cannot build our machines of it, for any sudden jar would smash them to pieces. A metal is reliable because it knows when to yield, and in yielding becomes even stronger. The art of compounding and heat-treating a metal to fit it for various mechanical tasks is a matter of nice compromise. We harden it by forging and hammering and mixing a metal with other metals, or putting carbon in iron, and go just as far as we dare while still preserving its ultimate power of yielding slightly under excessive strain. The peculiar atomic structure of a metal, the way the atoms can move past each other without breaking bonds, the way in which their relative positions can be altered by heat-treatment in the solid state, these are the qualities which make it so ideal a material for technology. We have only begun to explore the possibilities of creating new alloys with still more desirable properties. In the past great advances have been made in the metallurgical art by trying out various new combinations and discarding those which showed no improvement. The more we can pry into the fundamental factors which determine strength, the better the prospect of advancing more directly towards our goal and achieving even more spectacular successes in this age of metals.

The Royal Society of London
Part II

COLONEL SIR HENRY LYONS

In the second part of his account of the fortunes of the Royal Society, Sir Henry Lyons carries the story from 1820 to the present time. He shows that, as soon as scientific Fellows came to form a majority in the Council, the Society's influence on science rapidly grew, until now it is able to give powerful and beneficent help to the advancement of scientific knowledge.

In June 1820, shortly after the death of Sir Joseph Banks, the Council elected Dr W. H. Wollaston, the eminent chemist, to be President until the next Anniversary Meeting. He therefore presided at the Council meetings during the autumn, and certainly influenced the choice of members for the new Council, in which twelve out of the twenty-one were men of science; Sir Humphry Davy was nominated as President. It was a notable change of policy for the scientific Fellows to be in the majority, and Davy continued the practice, so that the councillors who were men of science varied from twelve to nineteen. Davy resigned, from ill health, in 1827 and was succeeded by Davies Gilbert, who strongly opposed all kinds of reform. His successor was H.R.H. the Duke of Sussex, the sixth son of King George III, whose election in 1830 was hotly opposed by many of the scientific Fellows, J. F. Herschel being put forward as an alternative candidate.

The Duke, however, was elected by a small majority and at once rendered the Society one important service: at the first meeting of Council at which he presided he proposed that the Treasurer's Report for 1829-30 should be printed and circulated to all the Fellows. This was done, and for the first time the Fellows were fully informed of the financial position of the Society, what sums had been received, and how their funds were being expended. Similar information has been given annually to the Fellows ever since, though it had not previously been available to any but members of Council. The misgivings of the scientific Fellows who were pressing for reforms were amply justified, and their criticisms could now be supported by irrefutable evidence.

The Council as now constituted became a much more active body than it had been in the past and the average attendance of its members rose at once. The Duke of Sussex was succeeded by Lord Northampton, an active geologist who had been for two years President of the Geological Society. Under his guidance the Council began to prepare plans for the reorganization of the Society, and in 1846 appointed a 'Charters Committee' with instructions to report what revision of the Charters was desirable, with a view to obtaining a supplementary Charter from the Crown. The Committee consisted of the President, the Vice-presidents and the Secretaries, to whom W. R. Grove, an

Sir John Herschel.
(By courtesy of the Royal Society.)

eminent mathematician and a lawyer of wide experience, was added.

After a careful study of the whole matter the Committee reported that no revision of the Charters was necessary, since the objects desired could be attained by a revision of some of the statutes, and to do this was within the powers of the Council. It had the additional advantage that necessary changes could be made without bringing the whole matter before a general meeting of the Fellows, at which those who were opposed to any reform would probably organize an active opposition. The Committee therefore proposed that: (1) the election of Fellows should take place on the third Thursday in June; (2) that the number recommended by the Council for election in each year should not exceed fifteen; and (3) that the names of all candidates proposed should be printed and circulated to all the Fellows in the first week in May.

In this way the right under the Charter of the Fellows as a body to elect as many as, and whomever, they pleased was not interfered with; but in practice the Anniversary Meeting has always accepted the names recommended by the Council. Previously, from twenty-five to thirty candidates —and occasionally as many as forty or fifty—had been elected annually, so the new procedure soon brought about a reduction in the number of Fellows, which had for many years been recognized as desirable. The fifteen candidates were selected by the members of Council, who were now almost all men of science, and this ensured that their qualifications were such as were needed to raise the scientific reputation of the Society.

The Committee, as well as the Finance Committee, reported on the effect that the proposed statutes might have on the income of the Society, and both reported that with due care the normal expenditure could be met. The new statutes were therefore approved by the Council on 10th February, 1847, and the first batch of fifteen candidates recommended for election was approved by a General Meeting of the Fellows in June 1848. Ten years later a Committee appointed to report on the working of the revised statutes recommended that the new procedure should be continued, as it had proved to be quite satisfactory.

In 1847 the number of Fellows was 764; by the end of 1860 it had fallen to 630, of whom 330 were scientific men, so that now for the first time these formed a majority in the Society.

There was much to be done to make the administration adequate to the new requirements. Much of the procedure hitherto in use needed revision. Particularly the increasing number of scientific Fellows, and the rapid growth of all branches of science at this time, resulted in a large increase in the number of scientific communications to be examined, and if accepted to be published in the *Philosophical Transactions* or the *Proceedings*. By 1860 much had been accomplished, and the Council, which now contained an average of nineteen men of science out of its twenty-one Councillors, was administering a Society mainly composed of scientists, and wholly devoted to the improvement of natural science. The aims of its founders were now well on the way to being fulfilled.

In 1861 General Sabine, the magnetician, was elected President; he held the position for ten years. By this time the Councils had come to the conclusion that a long tenure of the presidency was not in the Society's best interests; also, as the holders were now being selected from Fellows distinguished for their scientific work, it was difficult for them to devote their time to its needs for long periods. Sabine was succeeded by Sir Joseph Hooker, who stipulated that he should not be expected to hold the Presidency for more than five years, since his work at the Royal Gardens, Kew, was increasing. Such a period had already been suggested at the Council, and has subsequently been recognized as the limit of a President's tenure of office. No special restrictions were suggested for the other offices, and two of the Secretaries and two Treasurers held their posts for twenty years or more. There may have been good reasons for this at the time when many changes were being introduced, but in recent years their periods of office have been limited to ten years.

By 1857 the invested capital of the Society amounted to £30,000, but the amount received from annual subscriptions as the number of Fellows diminished became less, while the cost of printing and publishing the constantly growing number of important scientific communications in the *Philosophical Transactions* and the *Proceedings* was mounting. The financial position would have become difficult had not the extension of London westwards greatly increased the value of land in the village of Acton, where the Society owned about 35 acres. In 1880 the Council received an offer to purchase this land for about £32,000 and accepted it, thereby easing the financial position. By the end of the century

the value of the investments held for the General Fund was £81,000, while those of the Medal and Lecture Funds amounted to £46,000, received from a number of bequests. Dr Wollaston had started the Donation Fund in 1828 with the object of the income being used to advance scientific research. Since then other bequests for a similar purpose have been received, and the capital now amounts to £40,000. By 1900 the Society was therefore free from financial anxieties, and was in a position to assist research workers of merit by grants up to a total amount of £1,100 annually.

The work of the Council, both scientific and administrative, was now increasing rapidly, so much so that it was becoming more than the Council and the standing committees for Finance, Library, and Scientific Relief could deal with. The number of standing committees was therefore increased until, by the end of the century, there were twenty of them. A special group of eight scientific or sectional committees was appointed in 1896, and these greatly relieved the scientific work of the Council.

Sir Joseph Hooker.
(By courtesy of the Royal Society.)

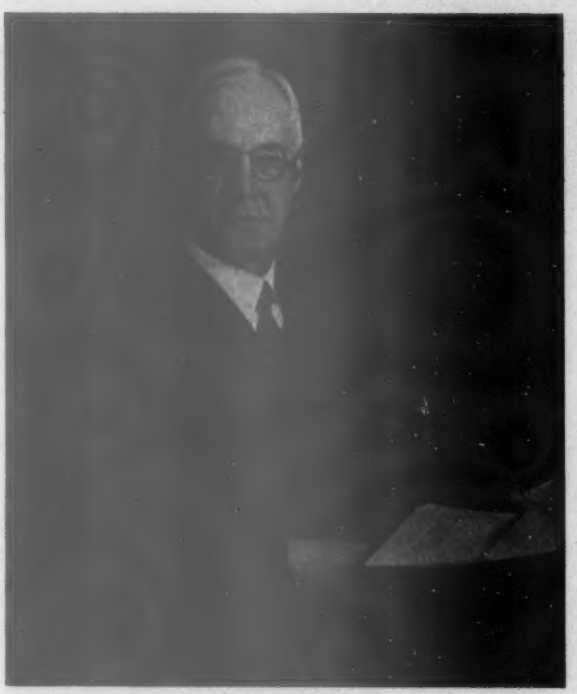
The Society has always maintained close relations with men of science in other countries. In 1742 it arranged to compare a yard measure and a pound weight with the corresponding measures in use in France, and sets of each were provided respectively for the Society and for the Académie des Sciences, Paris. In 1787, and again in 1821, the Society co-operated with French geodesists in carrying out with all the accuracy then attainable triangulation between the observatories of Greenwich and Paris. In 1836 von Humboldt wrote to the Duke of Sussex, then President of the Society, to seek his support in establishing stations for the study of terrestrial magnetism in England and her overseas possessions, and this he was able to arrange. From time to time representatives of Great Britain, usually nominated by the Society, served on other international scientific commissions.

In 1894 the Royal Society of Göttingen invited the Royal Society to send a representative to a conference at Innsbruck where gravitational observations would be discussed. This proposal was accepted, and led to another, made in 1898, that the Society should be represented at a meeting of the academies and scientific societies of Göttingen, Leipzig, Vienna, and Munich. The Council accepted the invitation and instructed their delegates that, regarding the question of the Royal Society's adhesion to a proposed Association of Academies, it should be made clear that such adhesion must be contingent on the Association becoming truly international by including other countries, especially France. This was agreed to, and the Royal Society was desired to ascertain the views of the Academies of Science at Paris and St. Petersburg, and of the Accademia dei Lincei at Rome. All expressed support for the proposal, and the International Association of Academies was formed. It was active for fourteen years but came to an end on the outbreak of war in 1914.

In 1857 the Society undertook the preparation of a Catalogue of Scientific Papers published after 1800. The cost of compilation was met from the Society's own funds, but the Government met the cost of printing and publication. The experience gained by 1900 showed that the cost of a similar publication for the next century was greater than could be borne by any private institution; it was therefore proposed to carry out the work by international co-operation. The matter was discussed by the delegates of a number of countries and it was agreed that the scheme put forward should be tried for five years: the Society agreed to take charge of the work and advanced the capital necessary for

printing, etc. So successful was the result that the scheme was continued for two more five-year periods; by then, however, the war of 1914-18 had broken out and publication had to be discontinued. In 1919 the international council met to review the situation and decided that publication should not be resumed; and in 1922 the executive committee asked the Society to allow the Treasurer to act as receiver and to wind up the undertaking. This was a lengthy business and was not completed until 1935 when, on the advice of the Society's chartered accountants, about £13,000 due to the Society was written off by the order of the Council.

In earlier times the amount of information which was given to the Fellows about the administration of the Society was very small, but in 1896 the Council decided that a volume should be published early in each year providing information on the membership and the Society's various activities. This year-book has since been published regularly in January of each year. In 1898 certain information which had been collected for the year-book but which changed rarely if at all, such as the texts of the Charters, was collected to form the *Record of the Royal Society*. This is published only occasionally, the latest edition (the fourth) having appeared in 1940. It was now the policy of the Council to keep the Fellows fully informed of the changes which were made from time to time in the administration, and if desirable to consult them—though the right of the Council to make laws and statutes on its own authority as given in the Charter remained. In 1915 the Council decided to circulate its *Report to the Society*, which is presented at the Anniversary Meeting to all the Fellows, and to discuss it at a special general meeting early in November; here it could be explained and suggestions considered. In 1916 the Council ordered that the list of candidates for the Fellowship should be laid before the sectional committees, at which the qualifications of candidates could be discussed. In 1918 it was ordered that before any new statute or any modification of an existing statute was approved it should be brought before a special meeting of the Society. In 1935 the Council decided that the annual reports of the research professors, Fellows and students who had been appointed by the Council, and whose expenses were met from any of the Society's research funds, should be added to the Council's report. In these ways, and by the publication of *Notes and Records of the Royal Society* once or twice annually, a considerable amount of information is now being made available to the Fellows regularly.



Sir Henry Dale.
(Present President of the Royal Society.)

In 1919 and some of the following years the Society received very considerable gifts or bequests, the income from which is to be devoted to research in some branch of science. By these gifts the total invested capital of the research funds had been increased by 1939 to about £550,000. With the income so derived the Society has been able to appoint some fifteen to eighteen research professors, Fellows, and students who can devote the greater part of their time to some branch of research approved by the Council.

When we see the great improvements which have been made in the administration of the Society, and the notable advances in science due to the efforts of its Fellows in the ninety-six years which have passed since the statutes were revised in 1847, we may confidently expect that even greater and more important advances will be achieved by their successors in the years which lie ahead.

Locust invasions and their control

A. D. IMMS

In many parts of Africa and Asia locusts are still the menace to crops that they have bee since the dawn of history. In recent years, scientific methods have been applied to the stud of these predatory insects and their mass migrations, and there is now good reason to hop for an effective counter-offensive.

Locusts belong to the family Acrididae which comprises the common or short-horned grasshoppers (figure 1). Several thousand species of Acrididae are known, but fortunately only a small number comes into the category of locusts. A locust may be defined as a species of short-horned grasshopper (figure 7), which, at times, becomes predominantly gregarious and migrates considerable distances in great swarms. The depredations of these insects have menaced the food supply of man ever since he adopted agriculture (figure 5). References to locusts and their activities occur in the writings of Pliny, and in many Chinese, Egyptian, and Greek texts, besides the familiar Biblical allusions. The earliest discovered record of these insects is stated to be a representation of a locust on the wall of an Egyptian tomb, dated about 2400 B.C.

The life-cycle of a locust is as follows. The eggs are deposited by the female below the soil in 'pods' or packets. In countries with a cold winter the eggs remain dormant throughout this season until the spring, when the young insects or 'hoppers' emerge. In the tropics they hatch within a few weeks of being laid, provided there is sufficient moisture. The difference between grasshoppers and locusts first becomes evident in the hopper stage: with the former the individuals are solitary or, in other words, each lives independently of the others, whereas in the latter they congregate in dense bands (figure 4). Further development consists in rapid growth, together with periodic moulting of the skin, which occurs four to six times before the adult insect appears. The whole cycle lasts for about a year in temperate climates, but in the tropics there may be two or three generations in a year. Locust hoppers betray mass movements in bands that may be spread over several square miles. Eating all in front of them, these hordes of individuals move relentlessly forward irrespective of obstacles. An impelling force urges this movement; it is not hunger, since they often leave a fertile zone to enter an arid one. Recent research has proved that these movements are dependent upon temperature and occur only when it is sufficiently high, while excessive heat, like too low a temperature, checks them. The winged adults, like the hoppers from which they have been transformed, also betray mass movements, since they take to the wing in vast swarms. These similarly are impelled into such activity by causes other than mere lack of food.

Two main phenomena have long stood in the way of a solution of the locust problem. First, the more or less irregular periodicity of the outbreaks: they are not annual events but recur in cycles of several years (figure 8). Anti-locust measures are speedily organized and their application may alleviate pressing needs, but they are usually applied too late, besides leaving the menace of subsequent swarms uncatered for. The second is that swarms may arise in one country and cause depredation in numerous other lands along their paths. Yet, however effective the measures taken in these individual countries may be, they have no bearing on the general situation, viz. the source of origin of the swarms. To quote one example, swarms of the Desert Locust commonly arise in India during the summer monsoon rains, and migrate to Persia and Arabia, where their progeny give rise to further swarms that may pass on to Soviet Asia, Palestine, Iraq, Egypt, and East Africa. Lack of fundamental knowledge, and of a guiding policy for anti-locust measures founded upon it, have, therefore, from time immemorial frustrated human efforts to cope with the menace (figure 6).

In 1921 B. P. Uvarov, of the Imperial Bureau of Entomology in London, advanced what has subsequently become known as the phase theory of locusts. Subsequent observations made in South Africa in 1932, both in the laboratory and in the field, by J. C. Faure, and by other workers elsewhere, have so fully corroborated the main

FIGURE 1 – *Acrididae or short-horned grasshoppers (actual size).* 1, Anacridium aegyptium, *Southern France.* 2, Oedipoda coelurescens, *Savoy.* 3, Psophus stridulus, *Tirol.* 4, Titanacris albipes, *Amazons.* 5, 6, Mecostethus grossus, *the largest English short-horned grasshopper.*

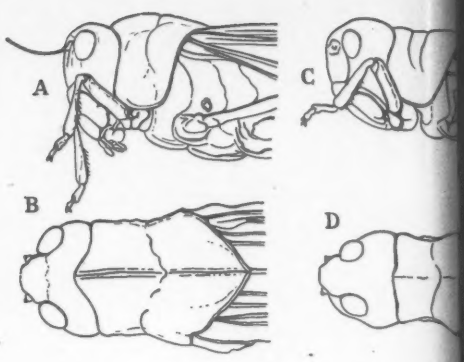


FIGURE 2 (*top left*) – *Showing the type of country an outbreak area of the Desert Locust on the Red of the Sudan.*

FIGURE 3 (*above*) – *Form of thorax in the African Locust.* A, B, *in the solitary phase;* C, D, *in the gre migratory phase.*

FIGURE 4 (*left*) – *Coco-nut leaves breaking weight of locusts settling on them: near Cebu, Islands.*

FIGURE 6 (*below*) – *A locust swarm: on the Kenya and Uganda.*

FIGURE 5 – *Hoppers of the Moroccan Locust on wheat: Caucasus.*

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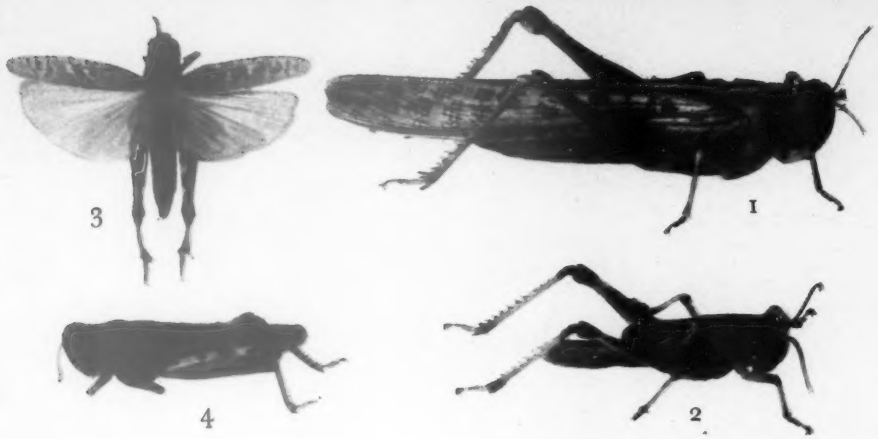

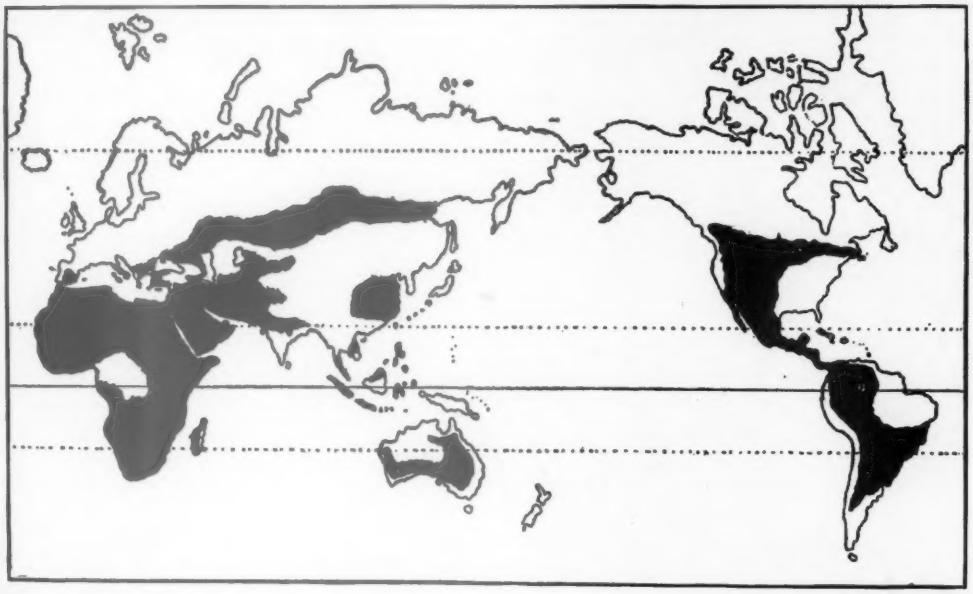

FIGURE 7 (*top*) – *Typical locusts* (*actual size*). 1, *Desert Locust* (Schistocerca gregaria), *winged adult.* 2, *Hopper of same, showing developing wings.* 3, *Italian Locust* (Calliptamus italicus): *Southern France.* 4, *Moroccan Locust* (Dociostaurus maroccanus): *Smyrna.*

FIGURE 8 (*middle*) – *Areas of the world subject to invasion by locusts and injurious grasshoppers shown in black.*

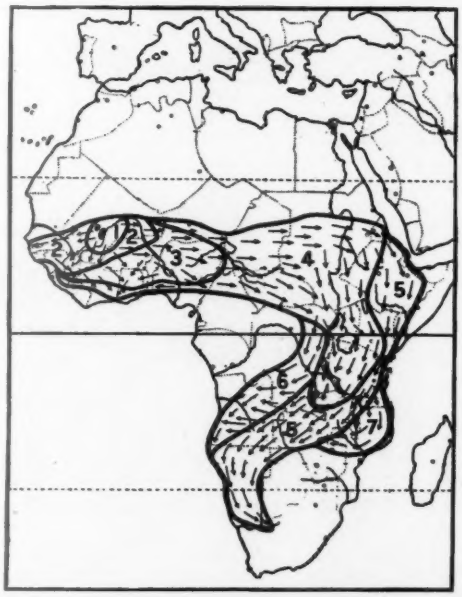

FIGURE 9 (*right*) – *Spread of the African Migratory Locust from where the outbreak originated in* 1928 *in areas marked by two spots in Zone* 1 *which was invaded in the first year. Zones* 2, 3, 4, *etc., represent the spread of the invasion in successive years up to* 1934. *Arrows indicate the main directions of the invasion.*

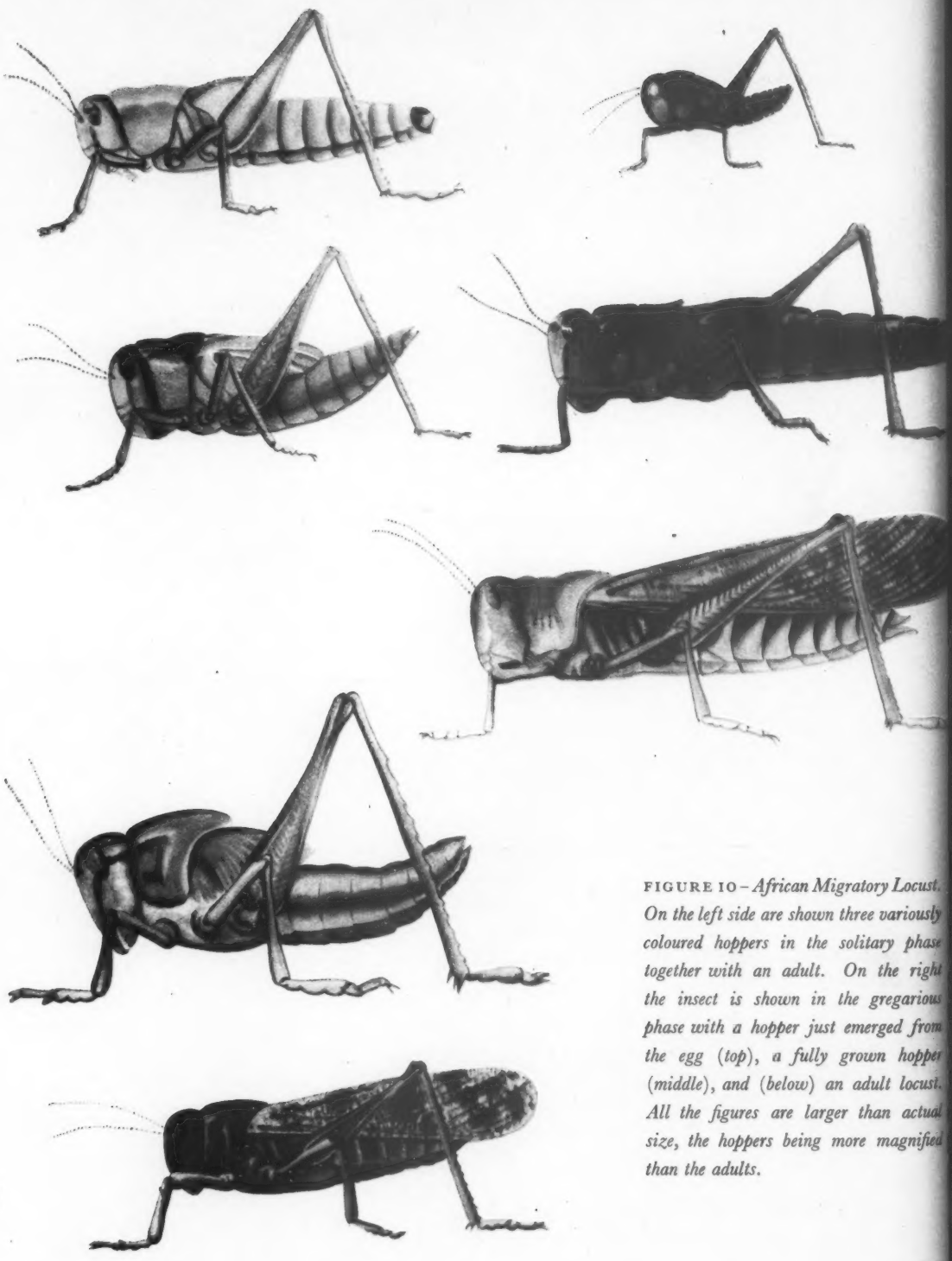

FIGURE 10 – *African Migratory Locust. On the left side are shown three variously coloured hoppers in the solitary phase together with an adult. On the right the insect is shown in the gregarious phase with a hopper just emerged from the egg (top), a fully grown hopper (middle), and (below) an adult locust. All the figures are larger than actual size, the hoppers being more magnified than the adults.*

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ntentions of Uvarov that his phase theory is re-rded today as an established biological phe-menon. The starting-point of the theory is at a locust can exist in three biological phases, z. a solitary one (*phasis solitaria*), a gregarious or igratory one (*phasis gregaria*), and a transitional e (*phasis transiens*). Taking the African Migra-ry Locust (*Locusta migratoria migratorioides*) gure 10) as an example, the *phasis gregaria* in its pper stages is constantly coloured black and ep orange-yellow. The adults have a short, nstricted pronotum (figure 3 C, D), and the tio of the length of the fore wing to that of the nd femur is equal to or greater than 2. In the *asis solitaria* the hoppers are variably coloured d tend to simulate the hue of their immediate ckground. The adults have a longer and oader pronotum with a dorsal keel (figure 3 A, B), d the wing/femur ratio is always less than 2. e *phasis transiens* is not represented by any defi-te form, but is intermediate in its characters tween the other two phases.

By varying the conditions, locusts can be reared perimentally from the eggs in such a way as to velop into whichever of the phases is desired. a large batch of hoppers be reared under owded conditions in a single cage they become tremely active and develop into a close approxi-ation to the gregarious phase. Under less owded conditions they display the *phasis tran-ns*, while individuals reared in separate con-iners grow into the solitary phase, the hoppers king on the general colour of their surroundings. e great activity and consequent high meta-lism of the gregarious individuals lead to the fferences separating them from those in the litary phase.

The periodicity of locust outbreaks is now known be connected with the transformation of these ects from the harmless solitary phase into the structive migratory one. This transformation curs in certain localized areas, known as *out-ak areas*, which have special conditions of mate and vegetation for each locust species. It here that the great swarms develop. In the rican Migratory Locust, swarms that arose out 1928, in a restricted area of the Middle Niger in the French Sudan, were the cause of an invasion involving a great part of Africa (figure 9). Some of the outbreak areas of the Desert Locust (*Schistocerca gregaria*) have been located in lands bordering the Red Sea (figure 2), while swarms of the Moroccan Locust (*Dociostaurus maroccanus*) develop on stony hillsides where vegetation is rather scanty. The extensive movements of locust swarms make it futile for each country to attempt its own isolated control measures; failure to repress these plagues has actually been due to isolationist policy. In 1928 a severe outbreak of the Desert Locust was the moving factor in causing the British Government to take steps towards coping with the problem by setting up a special research organization. This purely British venture led to the first International Locust Conference being held in Rome in 1930 (the fifth Conference was held in Brussels in 1938). This body requested the British organization to act as an international centre for collecting information and formulating research procedure. Today a special Anti-locust Research Centre in London operates under the supervision of Sir Guy Marshall, F.R.S., with Dr B. P. Uvarov as its technical organizer. Concerted investigations by parties of British, Belgian, French, South African, Egyptian, and Indian experts have collected a vast number of field data. Under great difficulties, the outbreak centres of locusts are being located and kept under observation—often in remote and inhospitable territories. By this means any tendency towards swarming can be noted and, at the same time, lands likely to be affected can be forewarned and so be in a position to apply timely measures. Ultimately, developing swarms may be destroyed in these centres, or the ecological conditions prevailing there may be altered by cultivation or other means so that they no longer give rise to locust swarms.

[Indebtedness for the use of figure 4 is to the Bureau of Agriculture, Philippine Islands. The Anti-locust Research Centre, London, allowed the use of figures 2, 5, 8, and 9; and figures 1, 7, and 10 are from specimens in the Cambridge University Museum of Zoology.]

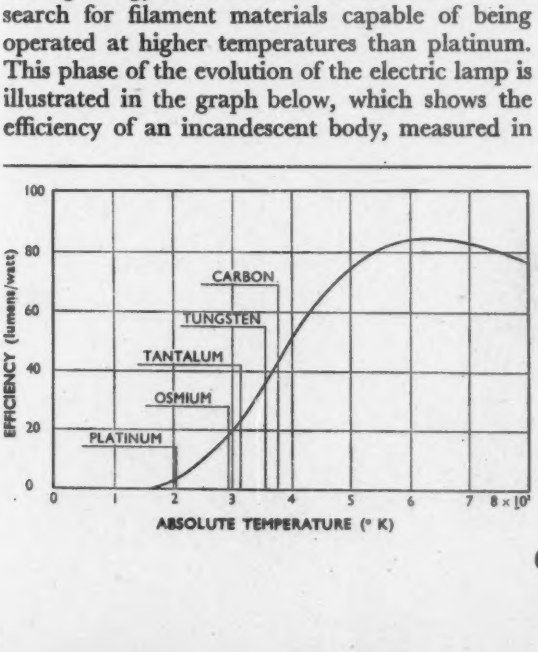
The evolution of the electric lamp

J. N. ALDINGTON

Many methods have been devised for the conversion of electrical energy into light. One of the earliest devices, namely Sir Humphry Davy's carbon arc, is still not without its usefulness, but modern scientific ingenuity has evolved a remarkably wide range of electric lamps of different kinds, adapted for every conceivable purpose. Mr Aldington describes some past achievements and outlines likely future developments.

Electrical energy can be converted into light by a variety of devices. A significant early event was Sir Humphry Davy's demonstration of the light produced by the carbon arc, which took place during a lecture at the Royal Institution early in the nineteenth century. It was not, however, until Faraday produced his electro-magnetic induction machine in 1831 that much real progress on electric lamps was possible. The development of means for readily producing electrical energy encouraged exploration of the possibilities of Davy's arc light, and it is interesting to note that carbon, used in the first experiments, is still the basis of arc lamp electrodes.

The discovery that thin wires could be heated to incandescence by the passage of an electric current led to the genesis of the first successful electric lamp of small size. As early as 1845 J. W. Starr demonstrated the production of light by the passage of an electric current through a platinum wire. Subsequent work was directed towards reducing energy losses from the filament and to the search for filament materials capable of being operated at higher temperatures than platinum. This phase of the evolution of the electric lamp is illustrated in the graph below, which shows the efficiency of an incandescent body, measured in lumens per watt, plotted against its absolute temperature. The melting-points of a number of elements which have been either suggested or used for the filaments of lamps are also indicated, although it must be appreciated that melting-point alone is not a sufficient criterion by which to judge the suitability of a filament material. For example, although carbon has the highest melting-point of any element its volatility at high temperatures greatly exceeds that of tungsten. Nevertheless, the success of carbon as the electrode of the arc lamp indicated promise of its being suitable for the filament of an incandescent lamp. Many different organic materials were carbonized in turn during repeated attempts to produce a refractory thin filament of suitably high resistance. It is no small tribute to the independent work of Swan in England and Edison in America that they eventually achieved success with such apparently unlikely materials as carbonized parchment, cotton thread, bamboo slivers, and best of all with a material not unlike the fibre of modern artificial silk (*see* figure 1).



The fact that a filament mounted in a bulb from which the air had been exhausted could be raised to incandescence more efficiently than a similar filament operating in air was appreciated about the middle of the nineteenth century. In the original work of both Swan and Edison the provision of an exhausted glass envelope enclosing the filament was further necessary because of the readiness with which carbon oxidizes when heated to incandescence in air. The skill of the glass-blower and developments in vacuum technique thus became essential elements in building the lamp industry. Such a standard of craftsmanship was established subsequent to the successful development of the carbon filament lamp announced in 1879 that very rapid progress was made (*see* figure 2, which shows different types of early carbon lamp).

The new industry had from the first attracted scientific workers, and the success which attended their labours led gradually to the establishment, in association with the industry, of research, development, and scientific control organizations of acknowledged repute. To this fact must be attributed the remarkable advances which have been made—particularly in the last decade—in methods of light production, and the advent of new and more efficient light sources.

It was about the beginning of the present century that Von Bolton and his colleagues worked out a process by which the refractory element tantalum could be drawn into thin wire. This development enabled Siemens and Halske to announce in 1903 the successful production of low-wattage lamps using tantalum filaments and operating at higher efficiencies than carbon lamps of similar size. The comparatively long and thin tantalum filament required supporting at a number of points and the method employed is shown in figure 3, in which a tantalum lamp made in 1905 is compared with a carbon lamp of 1882 due to Lane Fox.

During the period just reviewed, many attempts had been made to prepare filaments from tungsten —the most refractory of all metals. Success was eventually achieved in 1907 by squirting through diamond dies a paste made from finely divided tungsten powder and a volatile binder. The filaments so produced were bent into hairpin shape and, after a baking process to remove the binder, were mounted in series on to a number of V-shaped supports by arc welding. The resulting structure, illustrated in figure 4, was then sealed into a glass bulb subsequently exhausted of air. In spite of the fragility of the filament structure this first tungsten lamp, operating at an efficiency twice that of the carbon lamp, enjoyed considerable success until it was displaced by lamps using drawn tungsten wire.

In 1906 Coolidge began work with a view to producing ductile tungsten. It was known that fused tungsten, unlike other pure metals such as copper or gold, was very brittle and incapable of being worked into wire. The process eventually devised by Coolidge, and known as powder metallurgy, overcame this difficulty and enabled drawn tungsten wire to be produced for the first time. In the Coolidge process, tungsten powder containing a small percentage of some additive was shaped under hydraulic pressure into rectangular bars. By the passage of an electric current these bars were then 'sintered' (i.e. the discrete particles were made to cohere without complete fusion) at a temperature of about 3,300° K in an atmosphere of hydrogen. The fragile bars of pressed powder were thus converted into metallic rods of sufficient ductility to enable them to undergo, at about 1,500° K, the shaping process known technically as 'swaging.' The swaging operation was followed by hot drawing processes, by which wire of very small diameter was eventually produced. During these operations the plastic deformation of the crystal units developed during sintering resulted in a fibrous structure of great mechanical strength. The photomicrographs in figure 5, taken at a magnification of 500, illustrate the structure of sintered tungsten compared with that of the swaged bar and drawn wire.

A notable advance was made when Langmuir demonstrated in 1913 that the blackening of vacuum lamps was due to normal evaporation of the tungsten filament. He therefore suggested the use of an inert gas atmosphere in the bulb to reduce the rate of evaporation and to allow the filament to be operated at an increased efficiency. He showed that by using a coiled filament in place of a straight wire, the loss of energy occasioned by convection and conduction could be not only reduced but more than counterbalanced by the beneficial effect of the gasfilling, which permits operation of the filament at a higher temperature. While nitrogen at a pressure of approximately 1 atm. was used in the first experiments, the lower thermal conductivity of argon made the use of this latter element even more desirable. The production of argon on a commercial scale was therefore undertaken and the argon-filled lamp was marketed in 1915.

The coiled-coil[1] lamp which made its advent during the last decade followed in logical sequence from Langmuir's original work. By the production of a stable filament, shorter in length than the single coil filament of equivalent output, convection losses were reduced to an extent which allowed of a material increase in efficiency for the same designed life. At a still later date krypton was produced in sufficient quantity to enable it to be used with advantage, from the point of view of efficiency, for gasfilling certain types of special small lamps. Improvements in vacuum technique and the manufacture of special glasses, together with parallel developments in associated fields, have rendered possible the production of tungsten filament lamps of a great variety of types, operating at efficiencies many times that of

[1]See Figure 6.

the first carbon lamp. Typical examples of special projector lamps are shown in figure 7.

The earliest experiments on glow and arc discharges in gases and metallic vapours were stimulated by the fascination of the observed phenomena; the utilitarian aspect was hardly recognized. Indeed, it is only within the last two decades that results of outstanding commercial importance have been achieved. It was characteristic of early gas discharge tubes, which owed their luminosity to the positive column, that the brightness of the glow was extremely low and, in general, that a high voltage was necessary for their operation. The discharge tubes of Geissler, Crookes, Hittorf, and others, although little more than laboratory toys, were the forerunners of the Cooper Hewitt mercury vapour lamp (1900), the Moore carbon dioxide tube (1916), and the neon tube of Claude (1920). For a long time it appeared that the production of light by the electrical discharge was destined to be limited to tubular lamps of considerable size compared with tungsten filament lamps of equivalent light output. Development was given a new impetus, however, when it was found possible to apply the emissive alkaline earth cathode to gaseous discharge devices, a step which made possible the production of metallic vapour lamps of reasonable size and high light output, capable of striking directly on ordinary supply mains voltages. The first of such lamps to be made available for general illumination purposes employed a filling of sodium, and a necessary prerequisite of its successful development was the production of a special glass capable of withstanding the action of hot sodium vapour without darkening. The high efficiencies obtained with this lamp are due to the favourable position of the resonance radiation from sodium in relation to the peak of the visibility curve for the average eye. Commercial types of lamp of 85 watts and 140 watts rating have an initial efficiency of about 70 lumens per watt, practically the whole of the radiation being emitted at the wave-lengths 5,890–5,896 A.

The element which has proved most useful, however, for producing the vapour filling of modern discharge lamps is mercury, not only on account of its spectral characteristics, but also because of its comparatively low boiling-point. The last few years have witnessed a most varied series of developments in utilizing the properties of electrically excited mercury vapour under different conditions. A summary of the most important of these is given in the next column:

Mercury Vapour Pressures	*Lamp Type and Characteristics*	*Function*
C. 0·01 mm.	Mains voltage and high voltage tubing with inner surface coated with fluorescent powder. Low brightness and high efficiency	General and decorative lighting
C. 0·5 to 5·0 atm.	Mains voltage with hard glass or quartz discharge tube mounted in outer tubular envelope. High efficiency	General and street lighting
	Mains voltage discharge tube mounted in bulb coated with fluorescent powders. High efficiency and improved colour	General lighting where improved colour rendering is desirable
5·0 to 100 atm.	Mains voltage approximately spherical light source operating in quartz bulb. High efficiency and very high brightness	Projection work and to replace arc lamps
	High voltage linear source water-cooled. High efficiency and brightness	Projection work or where line source required

In the first group of lamps, in which the operating mercury vapour pressure reaches about 0·01 mm., the primary effect of the discharge is to produce mercury resonance radiation at the wave-lengths of 1,850 A and 2,537 A. This ultraviolet radiation is absorbed by, and thus renders luminous, a mixture of fluorescent powders coated on the inner surface of the tube within which the discharge takes place (*see* ENDEAVOUR, 1943, II, No. 5, 25).

The nature and composition of the fluorescent powder mixture can be controlled in such a way that the resultant light, produced at an efficiency of about 35 lumens per watt, has a quality very similar to that of the daylight sky. Alternatively, tubes exhibiting a wide range of colours can be produced, and these were made available in Great Britain some seven or eight years ago in the high-voltage pattern. It was not, however, until the advent of the mains voltage lamp, which was introduced in America in 1938 and in Britain in 1940, that the widespread adoption of fluorescent lighting was assured. For the present, manufacture in Britain is being confined to a fluorescent daylight lamp of 80 watts rating, but there can be no doubt that after return to normal conditions developments in both colour and lamp size may be anticipated. A characteristic and important feature of this type of light source is the low intrinsic brilliance, which in the case of the 80 watt lamp is of the order of 0·5 candle per square centimetre.

The light from lamps in the second and third groups is produced directly from the electrically excited mercury vapour. The correct working pressure is attained only after sufficient time has elapsed for the glass or quartz vessel in which the discharge takes place to reach a temperature

above the boiling-point of mercury. It is apparent, therefore, that the design of the lamp bulb must be such that its surface is substantially isothermal in order to avoid overheating of any section. Account must also be taken of the need for relating the allowable working temperature of the lamp bulb to the nature and properties of the material of which it is composed. Special borosilicate glasses have been developed for the 250 and 400 watt mercury lamps, and quartz is used for lamps of higher pressure where the temperature requirements are more stringent than even these glasses will tolerate. A typical lamp of the 400 watt type, developed primarily for street lighting, is shown in figure 8. The coefficient of expansion of the high silica-content glasses or of quartz itself is much lower than that of the special wires used for producing vacuum-tight seals used in incandescent lamp manufacture. It was found possible, however, so to relate the expansion-characteristics of the glass to those of tungsten or molybdenum that satisfactory direct seals could be made capable of operating at the high working temperatures (*c.* 500° C) which obtain in these lamps. The problem of producing direct hermetic seals through quartz was, however, much more complex, and has occupied several years. Its satisfactory solution has opened up new fields of development which have already yielded fruit in the form of extra high-pressure metal vapour lamps of extreme brightness.

It is significant that the spectrum of the mercury arc produced under the conditions of high vapour pressure and current density which obtain in certain modern lamps bears a strong resemblance to that of an incandescent body. This effect is shown in figure 9, where the spectra of mercury lamps belonging to the three main groups are compared. As the pressure is increased the position of maximum energy shifts from the resonance wave-length at 2,537 A towards the emission lines in the visible spectrum, resulting in an increase in the efficiency of light production. The possibilities of more effectively utilizing this phenomenon are by no means exhausted and work is proceeding.

FIGURE 1 (*top*) – *Left, Edison lamp*, 1879; *right, Swan lamp*, 1878.

FIGURE 2 (*middle*) – *Various carbon lamps*, 1880–90.

FIGURE 3 (*bottom*) – *Left, tantalum*, 1905; *right, Lane Fox*, 1882.

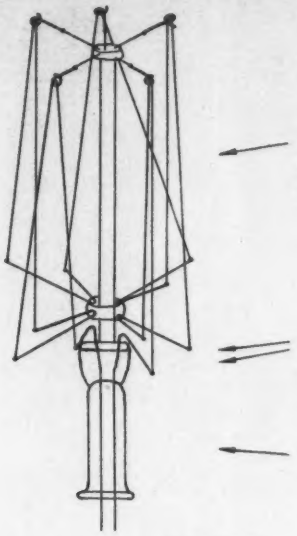


FIGURE 4

Sintered bar, 7 mm. square.

Swaged rod, 4 mm. diameter.

Drawn wire, 0·4 mm. diameter.

FIGURE 5

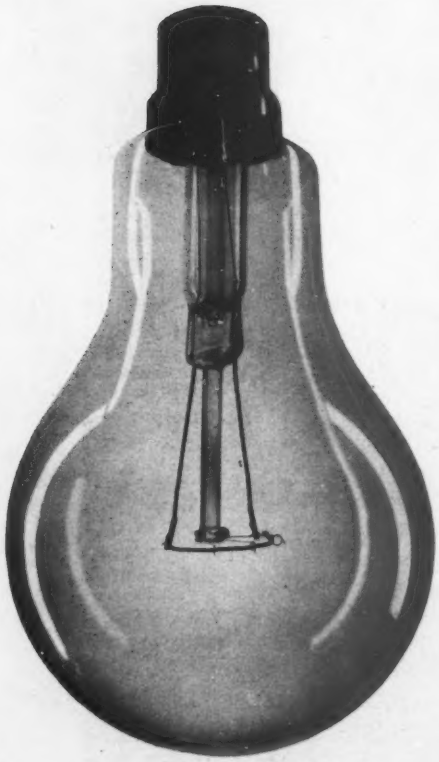
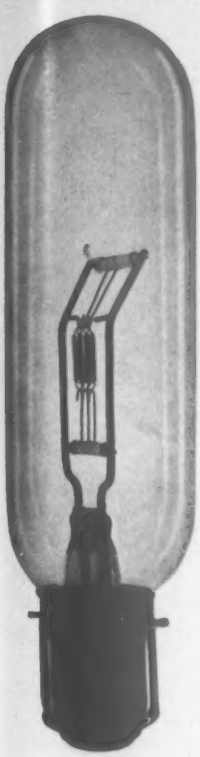


FIGURE 6 – *Coiled-coil lamp.*



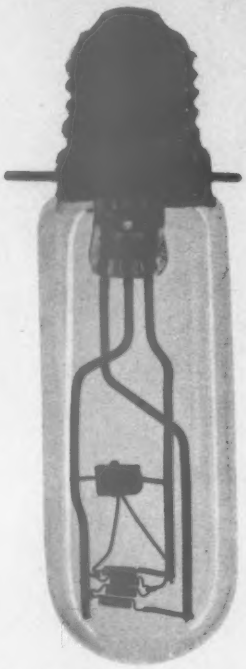


FIGURE 7 – *Projector lamps.*

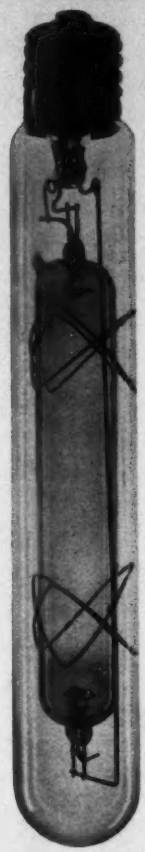


FIGURE 8 (*right*) – 400 *watt high-pressure mercury lamp.*

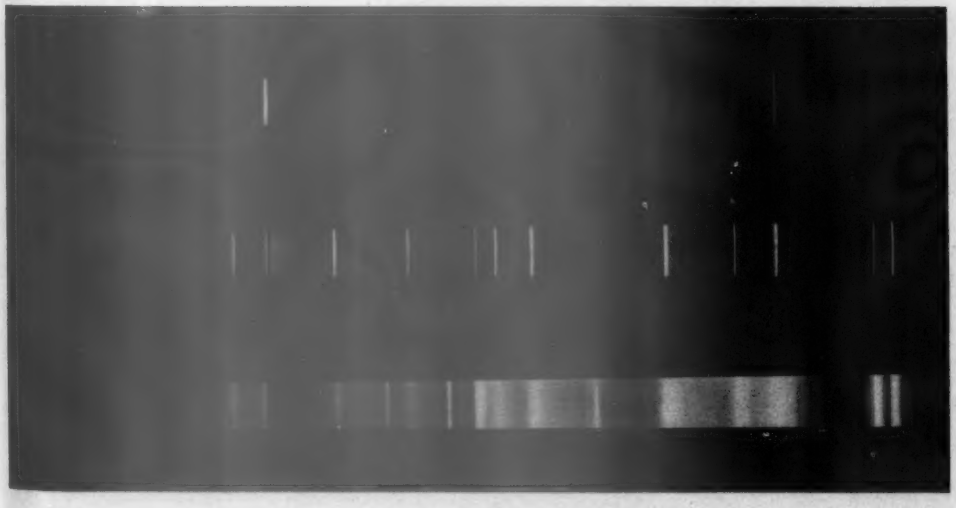


FIGURE 9 – *Spectra of mercury discharge at various pressures.*

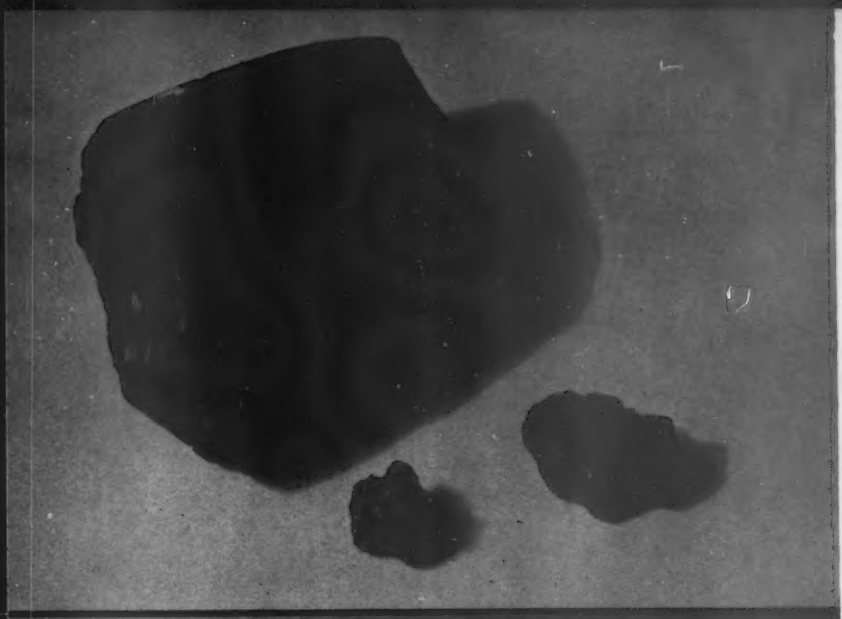


FIGURE 2 – *Crude hemp resin samples of Indian charas.*

FIGURE 3 – (*Above*): *hashish moulded into thin rods for insertion into cigarettes;* (*below*): *kif, chopped flowering tops from North Africa, for use mixed with tobacco in cigarettes.*

FIGURE 4 – *Marihuana cigarettes indicating one method of smuggling. The cigarettes are inserted into the folds of corrugated wrapping paper.*

The hemp drugs

A. R. TODD

The Assassins, Saracen sectarians notorious for their secret murder of Crusaders, owed their name to their practice of eating hashish as an intoxicant: an assassin is etymologically a hashish-eater. The chemical nature of the intoxicating principle in hashish has proved a difficult problem to solve. Professor Todd describes recent progress towards its solution.

Hemp (*Cannabis sativa*, L.) has been commercially important for thousands of years both for the fibre which it yields and for the oil obtained from its seeds. Knowledge that it produces an intoxicating principle is of almost equal antiquity, and the use of hemp preparations as medicaments, and more particularly as drugs of addiction, has long been prevalent in many parts of the world. The plant is an annual which can be grown almost anywhere from the temperate zone to tropical regions. It is dioecious, the male and female flowers occurring on separate plants, and the female flowering tops are covered with tiny glandular hairs which secrete a greenish resin believed by some to protect the ripening seeds. This resin, the active component of which also occurs in smaller amount in other parts of the plant, has a powerful physiological action and forms the basis of the various hemp drugs. The amount of resin produced and its activity vary considerably according to variety and the locality in which the plant is grown. Precise figures are difficult to obtain, but it is generally agreed that varieties grown in Asia (probably the original habitat of the plant) are the best producers of active resin. The varieties cultivated for drug production are generally smaller in size than those grown for fibre. The hemp drugs are known by a host of names according to locality and mode of preparation, i.e. whether prepared from the resin itself or leaves and tops, or from decoctions of the plant. Among the more common are *charas*, *ganja*, *bhang* (India); *hashish* (Egypt, Asia Minor); *kif* (North Africa); and *marihuana* (North, Central, and South America). Of these, hashish is perhaps the most familiar to European ears; it is indeed frequently applied as a kind of generic term for the hemp drugs. As most preparations of the type mentioned appear only on the illicit market, their precise mode of preparation is frequently rather obscure and their quality often uncertain.

FIGURE 1 – *Hemp* (Cannabis sativa). *Female flowering top.*

Historically, the use of hemp drugs was known in India two thousand years ago, and is so well established that the plant has assumed a divine status in some parts of that country. Curiously enough, although hemp has been applied medically in China since remote times, there is little evidence of its abuse in early records. The hemp drugs have long been used in the Near East, and have been a very serious problem in Egypt. They have never been much in evidence in Western Europe, and the use of hashish there is not recorded before the middle of the eighteenth century, when efforts were made to introduce it into medicine. The idea that the comparative absence of the vice from Europe was due to temperamental incompatibility is exploded by its spread in the United States, where, following the introduction of marihuana from Mexico, its abuse has advanced so rapidly that it is now a major drug problem in that country, and strict measures have been adopted to counter it.

Hemp preparations are usually eaten or smoked, the effects being, as might be expected, slower in developing when the preparations are eaten. To give an accurate picture of the effects of hashish is extremely difficult, partly because they are more subjective than objective,

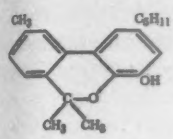
and because individual variation in response is probably greater with this than with any other drug. Many subjective descriptions of hashish intoxication are extant, but a number of the more widely known are based upon highly coloured accounts written by literary dabblers in the vice (e.g. the description given by Alexandre Dumas in *The Count of Monte Cristo*). It is for this reason that popular ideas of hashish effects are frequently erroneous. It seems clear that the primary effect of the drug is on the central nervous system and that peripheral effects are few. Among the commonest recorded effects are a feeling of well-being alternating with depression, distortion of time and space, and double-consciousness. Objectively there is a period of excitation and exaltation, followed often by sleep or coma. It is said that the taker of hashish suffers from no 'hangover' and that the drug, although it leads to moral deterioration, is not physically habit-forming, in the sense that there are no physical withdrawal symptoms such as are found in morphine addiction. Hemp preparations have been applied medically without a great deal of discrimination for a host of complaints with varying success, but they have fallen into disrepute mainly through the extreme variation in potency of the material employed, coupled with a lack of any reliable assay procedure and a general fear of addiction.

Until recently, exact scientific knowledge—both chemical and pharmacological—of the hemp drugs was very scanty. This is to be attributed to the rather intractable nature of the active resin, which long defied attempts by chemists to isolate pure substances from it, and to the lack of any animal test which was reliable and which gave results at all comparable with the effects observed in human beings. Since progress in chemical investigation of a drug is dependent on satisfactory biological testing, it is perhaps well to mention at the outset that two methods are used to assay hashish activity, one depending on the ataxia produced in dogs and the second on production of corneal anaesthesia in rabbits by intravenous injection (Gayer test). The relative potencies of various preparations are not always strictly parallel when measured by these tests, and the relationship between them requires further study. Recent work indicates that potency in dogs as measured by the ataxia method closely parallels that observed in human beings.

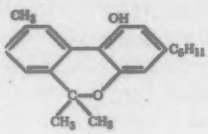
Chemical investigation of the hemp drugs has been carried on sporadically for nearly a century, the starting material being in all cases the resinous active material extracted from prepared drugs or from the plant source. It was found as early as 1857, by the brothers T. and H. Smith, that the hashish activity resided in the alkali-insoluble high-boiling portion of the resin, and that it was nitrogen-free—a surprising discovery since most people at the time expected the active principle to be, like those of opium and tobacco, an alkaloid. Later on, between 1895 and 1900, Wood, Spivey and Easterfield, and Dunstan and Henry, isolated from the active portion of the resin prepared by vacuum distillation a homogeneous viscous oil yielding a crystalline acetate. To it the name cannabinol was applied and some preliminary examination of it was carried out; but little real progress was made for another thirty years, when Cahn, in a series of elegant researches, went far to clarify its structure, and incidentally indicated that it was probably not, as had hitherto been assumed, the active principle of hashish. The absence of progress in the intervening period seems to have been due in the main to the fact that the various investigators who endeavoured to follow up the earlier work either failed to repeat the isolation of cannabinol or were deceived by the relatively narrow boiling range of the crude active resin into assuming it to be homogeneous. Between 1932 and 1934 Cahn established the carbon skeleton and the nature of the substituent groups in the molecule of cannabinol, and proposed for it structure (I) in which only the positions of the hydroxyl and *n*-amyl groupings remained uncertain. Unfortunately Cahn's researches were broken off at this stage and several years passed before the active resin was again studied. Since 1938 extended investigations by Todd in Great Britain and Adams in America, with their collaborators and associated pharmacologists, Macdonald and Loewe, have thrown a good deal of light on the subject. The British workers have used as sources of material mainly Indian hemp resin in the form of ganja and Egyptian hashish, while the Americans have used marihuana.

It was quickly found that cannabinol could be readily isolated from the distilled active resin from Indian ganja as its crystalline ester with *p*-nitrobenzoic acid, and that it was devoid of hashish activity, the active principle remaining in the non-crystalline portion of the esterified resin. From the fact that cannabinol gave a positive indophenol reaction showing that the *para*-position to the phenolic hydroxyl group was unsubstituted,

and from the results of nitration, it was deduced that of the twelve structures for cannabinol which were possible from Cahn's results only (I) or (II) could represent that substance.

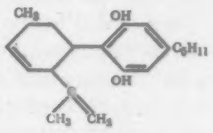


(I)



(II)

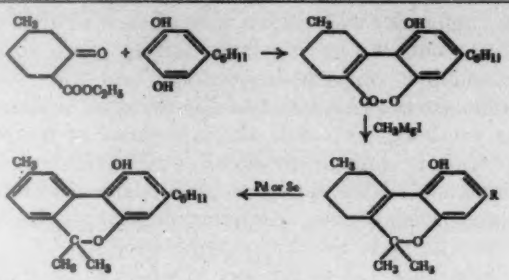
A decision between these two formulae became possible through the isolation and study of another constituent of hemp resin. In working up resin from marihuana, Adams isolated a dihydric phenol to which he gave the name cannabidiol. Simultaneously, Jacob and Todd, in the course of work on Egyptian hashish, observed that crude cannabinol from this source was contaminated with a second phenol which proved to be identical with cannabidiol from marihuana. It is of some interest to note the variation in the content of cannabinol and cannabidiol in drugs of different origin. The Indian drug seems to contain very little cannabidiol and the American little cannabinol; Egyptian hashish occupies a midway position in this respect. Cannabidiol, like cannabinol, is devoid of hashish activity, and is the substance mainly responsible for the *Cannabis* reaction known as the Beam test (purple coloration with alkali); available degradative evidence suggests for it the structure (III) although it has not yet



(III)

been synthesized in the laboratory. The orientation of the hydroxyl groups in cannabidiol, proved by the production of olivetol (5-*n*-amylresorcinol) from it by pyrolysis with pyridine hydrochloride, together with the simultaneous occurrence in hemp of cannabidiol and cannabinol, led to the conclusion that the molecular structure of the latter must be represented by (II). This conclusion was verified by two independent and wellnigh simultaneous syntheses of cannabinol by Adams, Baker, and Wearn, and by Ghosh, Todd, and Wilkinson.

The synthetic method of the latter workers, indicated schematically above, is of particular



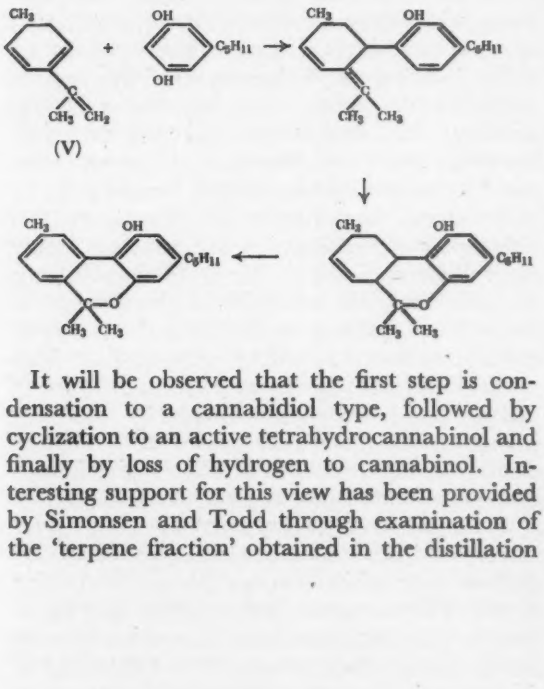
(IV)

interest because the intermediate tetrahydrocannabinol (IV; R = *n*–C_5H_{11}) has been found to show the typical physiological effects of hashish in rabbits, in dogs, and in man. With a view to establishing the structural features necessary for exhibition of this activity, a large number of analogues of synthetic tetrahydrocannabinol in which the molecule was modified in various ways has been synthesized by this method both in Great Britain and in America. While the results of these studies cannot be discussed in detail here, it is interesting to note that in homologues of (IV), where only the group R varies in size, activity in the *n*-alkyl series rises from methyl to a maximum at *n*-hexyl, and then decreases again. The synthetic tetrahydrocannabinol (IV; R = *n*–C_5H_{11}) as ordinarily obtained is, of course, optically inactive, whereas it is known that the natural physiologically active resins are strongly laevorotatory. By using suitable starting materials, however, the pure dextro- and laevorotatory forms have been synthesized and the latter shown to be several times more active than the former, although still considerably less so than highly purified natural resin. The synthetic substance we have been discussing is not the only tetrahydrocannabinol to show hashish activity. Adams has shown that by heating with acid catalysts cannabidiol (III) is converted to a mixture of highly active tetrahydrocannabinols differing from each other and from synthetic tetrahydrocannabinol in the location of the ethylenic linkage in the left-hand ring, or stereochemically, or both.

The isolation of the homogeneous active principle from hemp resins freed of terpenes, hydrocarbons, cannabinol, and cannabidiol has proved a very difficult matter. From Indian and Egyptian material products have been obtained with physiological potency greater than that of any of the synthetic substances mentioned above. Analysis of these various products suggests that they are isomers of synthetic tetrahydrocannabinol, and,

in conformity with such a view of their structure, they contain one ethylenic linkage and yield cannabinol on dehydrogenation. As they are resins from which no crystalline derivatives have as yet been prepared, absolute proof of homogeneity is difficult to obtain. All evidence at present available, however, justifies the view that hemp resins contain a mixture of physiologically active isomeric tetrahydrocannabinols.

Speculation as to the way in which physiologically active substances are elaborated in plants is always attractive, and some attention has been given to this in the case of the typical hashish constituents. Examination of the formula of cannabidiol (III) shows that scission of the bond linking the two rings would leave on the left a substance belonging to the terpene group of natural products which form the major constituents of essential oils, and on the right olivetol, a common constituent of the class of plant products known as depsides. This leads to the suggestion that cannabidiol, tetrahydrocannabinols, and cannabinol may arise in nature from the condensation of a terpene derivative with olivetol. A hypothetical scheme of biogenesis is outlined below.



It will be observed that the first step is condensation to a cannabidiol type, followed by cyclization to an active tetrahydrocannabinol and finally by loss of hydrogen to cannabinol. Interesting support for this view has been provided by Simonsen and Todd through examination of the 'terpene fraction' obtained in the distillation of Egyptian hashish. The lower-boiling portion consisted mainly of *p*-cymene and methyl-4-isopropenylbenzene. Now a menthatriene (V), if it existed as a synthetic intermediate in the plant, would be unstable and would probably be converted by isomerization or dehydrogenation into these two compounds which are actually found in bulk in the resin. It is worth noting, too, that the hypothetical scheme outlined gives a rational explanation of the variation in composition and potency of hemp resin obtained from different localities.

Efforts have, of course, been made to realize at any rate parts of the above scheme of biogenesis in the laboratory. The conversion of cannabidiol to active tetrahydrocannabinols and of tetrahydrocannabinol to cannabinol has already been mentioned. As regards the initial stage, the menthatriene (V) is rather inaccessible, but by condensing the readily available terpene derivative *d*-pulegone with olivetol, a physiologically active product has been obtained from which the dextrorotatory form of the tetrahydrocannabinol (IV; $R = n\text{-}C_5H_{11}$) has been isolated. This compound is accompanied in the product by at least one other inert substance which is probably a xanthene derivative; whether substances like the latter are also present in hemp resin is as yet unknown.

Such, then, is a general outline of the present position regarding scientific investigation of hashish. It is clear that much further chemical and pharmacological work remains to be done before complete understanding is attained, but the foundation for such an understanding would appear to have been laid. On the practical side, too, the fact that pure synthetic substances showing the typical activity of *Cannabis* are now available will, it is hoped, lead to their clinical examination and possibly to the discovery of medical applications for this interesting group of compounds.

In conclusion, the author would like to acknowledge here his indebtedness to Mr F. Thornton of the Home Office (Drugs Branch) for facilities to obtain the illustrations reproduced in this article and for his co-operation in the course of many of the researches discussed.

Vitamin D

LADY MELLANBY

Lady Mellanby was present at the birth of vitamin D in 1918, and might indeed be regarded as midwife and nurse to a baby born after a difficult labour and scornfully received. Here she describes its development into a lusty adult of enormous importance to human welfare, but adds that vitamin D is still the greatest single deficiency in the diet of Britain.

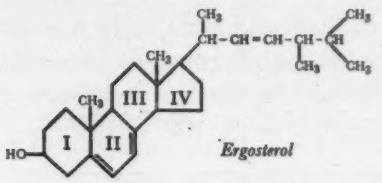
When it was discovered by experiments on puppies, made in England during the first world war, that rickets was a disease due to insufficiency in the diet of an antirachitic or calcifying vitamin which was 'either identical with fat-soluble A or has a natural distribution somewhat similar to vitamin A,' a remarkable chapter of scientific investigation was begun, which continues to this day. The discovery had widespread influence, partly because of its great practical implications. In the first place, it provided the immediate means of preventing and curing rickets (see figure 1), one of the commonest and most deforming diseases of Western civilization. Secondly, it opened up a new chapter of dental science by showing that the structure of the teeth depended on specific substances in the food eaten during the time of their development, and especially upon the intake of a calcifying vitamin. This is illustrated in figure 2.

The practical significance of the discovery was not, however, sufficient in itself to explain the great interest of scientific workers. To account for this, further explanation is necessary. Announcement of the presence of a calcifying vitamin in certain foods such as cod-liver oil, egg-yolk, milk, and some animal fats was at first met with much incredulity. Medical men did not believe that there was such a vitamin, but thought that rickets was mainly due to lack of hygiene, emphasis being put on confinement and insufficient exercise; massage and electrical treatment were often recommended to overcome the disease. Although none of these factors *per se* proved to be of major importance in rickets, hygiene did indeed play a part, as was shown when Huldschinsky discovered that rickets was cured by the exposure of the skin of babies to the ultra-violet radiations of a mercury-vapour lamp. The next few years were occupied in bringing together these two apparently remote factors controlling bone and tooth calcification—a fat-soluble vitamin (the dietetic factor) and something produced by ultra-violet radiations acting on the skin (the hygienic factor).

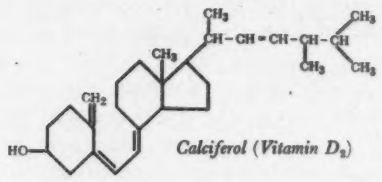
It is not necessary to repeat the well-known story leading up to the discovery that the beneficial effects of ultra-violet radiations from the mercury-vapour lamp and from the sun were also due to a calcifying vitamin and that, in fact, these radiations were of value simply because they transformed an inactive sterol—the provitamin of the skin—into an active vitamin. This phenomenon was at the time something quite new in physical and biological science, and it elucidated the hitherto unsolved problem as to why the native children in tropical zones rarely developed rickets and dental caries, whereas both diseases were so prevalent in temperate zones. It became evident that, though the diets of the tropical natives were often deficient in the calcifying vitamin, perhaps even more so than in temperate zones, they really had ample supplies because of the action of sunlight on the provitamin of their little-clad bodies. The Eskimos in the arctic regions, on the other hand, had straight, hard bones and beautiful teeth because of the calcifying vitamin in the fat of their food. It was later shown that many foods, including cereals, also contained a provitamin which could be activated by exposure to ultra-violet radiations. The beneficial effect on the teeth of food treated in this way is seen in figure 3.

Much information was gradually obtained about the actual transformation of ergosterol, by ultra-violet radiations, into the calcifying vitamin, now called vitamin D. The change was shown to involve the formation of a series of chemical substances: ergosterol → lumisterol → protachysterol → tachysterol → vitamin D (in Britain often referred to as calciferol). Calciferol itself was also liable to be broken down further to inactive substances—toxisterol and suprasterols I and II. It was found to be an isomer of ergosterol, and the effect of the ultra-violet radiations was to open

up the phenanthrene nucleus between carbon atoms C_9 and C_{10} in ring II, the formulae of the two substances being:



Ergosterol



Calciferol (Vitamin D_2)

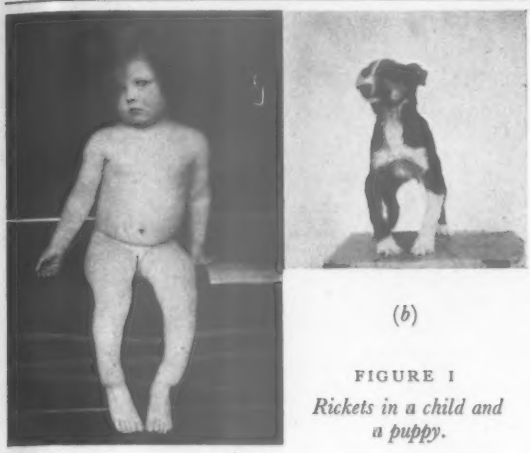
Chemists next proceeded to show that the activation of ergosterol into a calcifying vitamin was only one of a number of similar reactions. At least nine other sterols were found to act as provitamins D and to be transformed into substances with powerful calcifying actions by exposure to the same part of the ultra-violet spectrum as that which converted ergosterol into calciferol, namely wave-length 260–300 mμ, and in each case the active substance was isomeric with the parent substance.

Fortunately the physiological problem was simplified to some extent by the acceptance of the fact that, although this was a vastly interesting study to the chemist, only two of the provitamins were of important biological interest, viz. ergosterol and 7-dehydrocholesterol. It is now usual to call the vitamin produced from ergosterol (calciferol) vitamin D_2, and that from 7-dehydrocholesterol vitamin D_3. (Vitamin D_1 is the molecular addition product of D_2 and lumisterol.) Vitamin D_3 bears the same chemical relationship to 7-dehydrocholesterol as vitamin D_2 does to ergosterol. The ring structure of vitamin D_2 (given above) and D_3 is identical, but the side-chain of the former is that of ergosterol and of the latter that of cholesterol.

So long as ergosterol was the only known provitamin D, it was assumed that the vitamin D of vegetable and animal life was activated ergosterol. There is no evidence that the vitamin can be formed in higher animals in any other way than by ultra-violet radiations acting on a provitamin in their skin. All present experience indicates that, if animals get no vitamin D in their food and are not exposed to ultra-violet radiations, they will suffer from the specific ills due to vitamin D deficiency. Fish, which are naturally beyond the influence of ultra-violet radiations, were therefore supposed to get their vitamin D from plankton and algae which, floating on the surface of the sea, had been exposed to sunlight; cows got their vitamin D either from grass exposed to sunshine or from the effects of sunshine on the provitamin in the skin. These hypotheses were shaken by the discovery that the main vitamin D of vertebrate animal life was not activated ergosterol (vitamin D_2) but activated 7-dehydrocholesterol (vitamin D_3). There remains indeed a gap in our knowledge concerning the relation of the vegetable provitamin, ergosterol, to the chief animal provitamin, 7-dehydrocholesterol.

So far as is known at present, vitamins D_3 and D_2 have similar modes of action in the human body; vitamin D_2, however, has little effect on bone formation in birds, and for this reason the poultry farmer gives a fish-liver oil to his chickens rather than irradiated ergosterol. Incidentally it may be remarked that the dog breeder and poultry farmer were comparatively quick off the mark in using the new therapy.

Vitamin D seems to have two general effects in the body, although both may be due to one type of action. In the first place it facilitates the absorption of calcium and phosphorus from the alimentary canal, so that a more plentiful supply of these elements is available to the tissues. Thus, if a diet free from vitamin D is taken, as the body stores of the vitamin are gradually reduced progressively smaller quantities of calcium and phosphorus are absorbed and greater quantities are excreted in the faeces. At first this lack of vitamin D in the food can be overcome by increasing the calcium and phosphorus intake; but when all the body stores of the vitamin are lost, this compensation tends to break down and the additional elements are rejected. The vitamin also appears to control the incorporation of the calcium and phosphorus carried by the blood into the tissues of the developing bones and teeth. Present evidence suggests that, in the absence of vitamin D from the body, even if the necessary calcium and phosphorus were injected directly into the bloodstream, little or none would be incorporated in the tissues needing them. In other words, vitamin D appears to be the key to the availability of calcium and phosphorus in the tissues; when there is abundance of this vitamin in the body, good



(*a*) (*b*)

FIGURE 1
Rickets in a child and a puppy.

(*a*) *A child with rickets, as evidenced by some bowing of the legs and swelling and deformity of the wrists and ankles. Very much worse cases of the disease were seen in industrial areas before and during the first world war.*

(*b*) *A puppy with experimentally produced rickets roughly corresponding in degree to that of the child in* (*a*). *The diet of the puppy was deficient in the calcifying vitamin D. A similar diet with the addition of the vitamin results in a normal, straight-legged animal.*

The addition to the diet of either the child or the dog of $\frac{1}{20}$ *mg. of vitamin D daily* (*i.e. double the preventative dose* [*see p.* 78]) *would result in time in the straightening of the legs.*

bones and good teeth can be procured even with remarkably small supplies of these elements in the food and water.

The compounds of calcium and phosphorus in the food are not all equally available to the body. Indeed there is one important dietary constituent, phytic acid (inositol hexaphosphoric acid), which actually interferes with calcification by precipitating calcium in the gut and making it unavailable. The photographs of three puppies in figure 4 show this clearly. Under some conditions, and especially when vitamin D is deficient, phytic acid in the food can even deprive adult bones of their calcium and produce osteomalacia, a disease—characterized by a gradual softening of the bones—not often seen in England but common in the East. However, vitamin D can effectively clip the claws of phytic acid and even cause much of its phosphorus to be absorbed and to be beneficial rather than harmful. This fact is illustrated in figure 5. Phytic acid is abundant in cereals, especially in oatmeal and maize. The fact that cereals form such a large part of the British diet, which is often deficient in vitamin D and calcium, is one of the main reasons why our bones and teeth are so badly formed and why it is necessary to

Molar teeth of four children. *Molar teeth of four dogs.*

(*a*) (*e*)
(*b*) (*f*)
(*c*) (*g*)
(*d*) (*h*)

FIGURE 2 (*right*) – *Enlarged photographs of the surface enamel of human and dogs' molar teeth.*

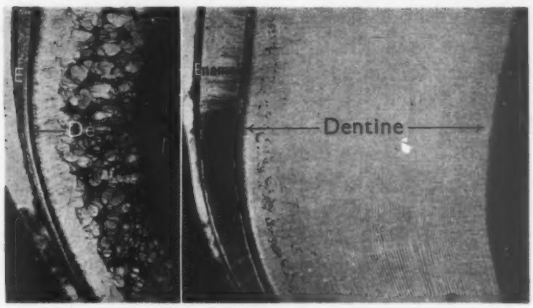
(*a*) and (*e*) *Good structure; smooth and shiny.*

(*b*) and (*f*) *Slightly defective structure; some roughness.*

(*c*) and (*g*) *Very defective structure; rough.*

(*d*) and (*h*) *Grossly defective structure; comparatively large areas of deficient enamel.*

The dogs from which the teeth (*e*) *to* (*h*) *were taken had different amounts of fat-soluble vitamins, especially vitamin D, the dosage being progressively reduced, so that* (*e*) *had an abundant supply and* (*h*) *very little. By analogy, and on the basis of a few investigations on children whose diets were controlled, it seems reasonable to assume that the different types of enamel in these human teeth* [(*a*) *to* (*d*)] *are also due in the main to variations in the fat-soluble vitamins, and especially vitamin D, available at the time of their development.*



(*a*) (*b*)

FIGURE 3 – *The effect of ultra-violet light on the provitamin in cereals.*

Photomicrographs of sections from comparable parts of the molar teeth of two litter-mate dogs. Both had the same vitamin D-deficient diet, but the cereal of (*a*) *was untreated, while that of* (*b*) *was exposed to ultra-violet radiations.*

Note *in* (*a*) *the thin and poorly calcified enamel and dentine compared with the tissues in* (*b*). *The dark, irregular areas in the dentine represent poorly calcified tissue.*

(*a*) (*b*) (*c*)

FIGURE 4 – *The effect of phytic acid of oatmeal in the absence of vitamin D.*

Photographs of three puppies of one litter living under the same conditions. Their diets were similar, except as mentioned below, and all contained vitamin A, but were deficient in vitamin D.

(*a*) *had white flour which contained very little phytic acid.*

(*b*) *had oatmeal which contained much phytic acid.*

(*c*) *had white flour to which was added phytic acid extracted from oatmeal, in amount equivalent to the phytic acid in the oatmeal fed to* (*b*).

Note: (*a*) *has very little rickets, while* (*b*) *and* (*c*) *are very rachitic to about the same extent. The addition of vitamin D to any of these diets would have resulted in a normal, straight-legged dog.*

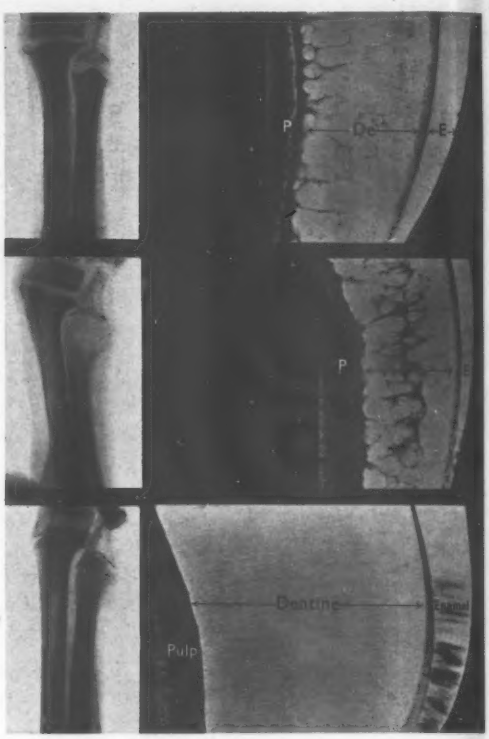


FIGURE 5 – *Phytic acid antagonized by vitamin D.*

X-ray photographs of the wrist-joints and photomicrographs showing sections from comparable parts of the teeth of three litter-mate dogs kept under identical conditions. All had a diet deficient in vitamin D but containing vitamin A.

(*a*) *had no additions.*

(*b*) *had 200 mg. of phytic acid added daily.*

(*c*) *had 200 mg. of phytic acid together with 2,000 international units of vitamin D added daily.*

The X-ray photographs show a medium amount of rickets in (*a*), *much in* (*b*), *and none in* (*c*).

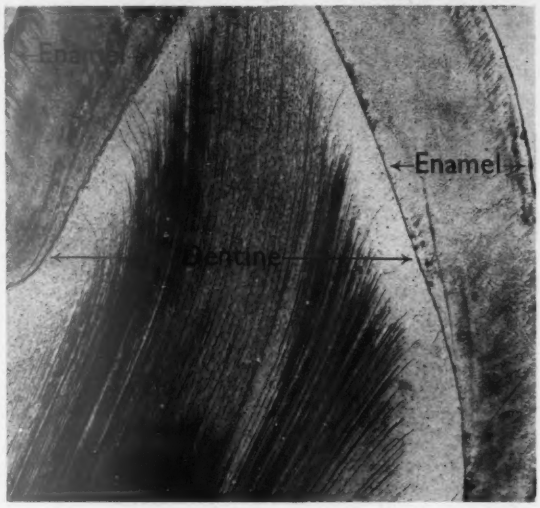
The photomicrographs of the teeth show that in dog (*b*) *the addition to the diet of phytic acid has resulted in thinner enamel* (E) *and thinner and less well-calcified dentine* (De) *than are found in* (*a*). (*This is indicated by an increase in the dark, poorly calcified areas.*) *The addition of vitamin D to the diet of* (*c*) *has more than counterbalanced the harmful effect of the phytic acid. The dentine of the tooth is thick and the structure is good, with none of the dark, poorly calcified areas so evident in* (*b*), *and appearing to some extent in* (*a*).

FIGURE 6 – *The effect of fat-soluble vitamins A and D on the teeth. Photomicrographs showing sections from comparable parts of teeth of three litter-mate dogs kept under identical conditions. All had oatmeal, separated milk powder, lean meat, orange-juice, yeast, and salt in their diet.*

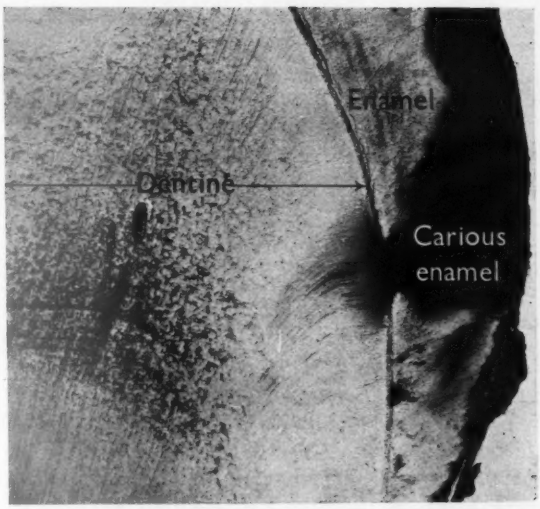
(*a*) *had an addition of fat-soluble vitamins in the form of cod-liver oil for the experimental period of five months. Both enamel and dentine are thick and well formed.*

(*b*) *had olive oil instead of cod-liver oil throughout the same experimental period. Both enamel and dentine are thin and the dentine is ill formed, with many poorly calcified areas (shown in black in the illustration).*

The diet of (*c*) *was devoid of fat-soluble vitamins for five months and then cod-liver oil was given for one month. The dentine laid down in the first period is very similar in amount and structure to that of* (*b*), *whereas that deposited in the last month is almost as thick as that laid down in the first five months and is as well formed as that of* (*a*).



(*a*)



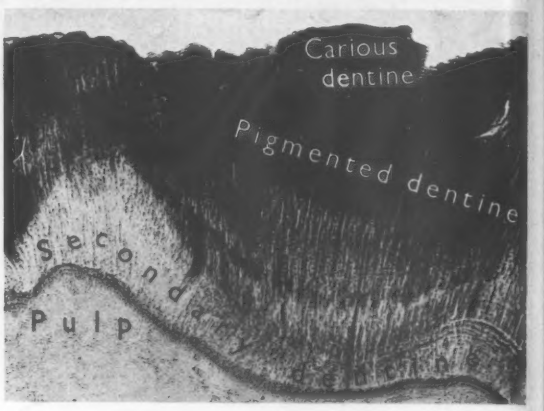
(*b*)

FIGURE 7 – *Photomicrographs of sections from comparable parts of molar teeth of two children, showing different types of histological structure.*

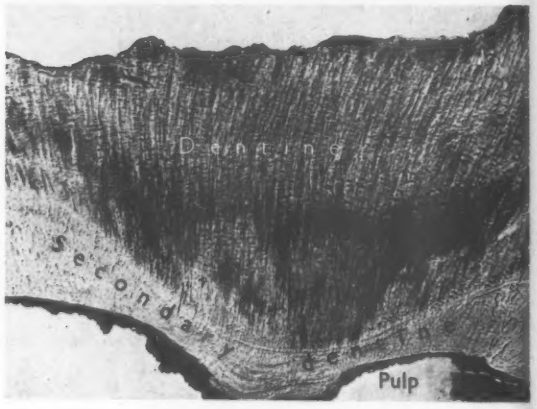
(*a*) *Good structure; no poorly calcified areas in the dentine.*

(*b*) *Defective structure; many poorly calcified areas in the dentine (dark patches in the illustration).*

(*a*)



(*b*)



(*c*)

FIGURE 8 – *The "healing" of dental caries.*

(*a*) *and* (*b*) *Photomicrographs of sections of teeth extracted from a child,* (*a*) *before daily supplements of vitamin* D_2 *and* (*b*) *after nine months' vitamin* D_2 *therapy. The child was* $3\frac{1}{2}$ *years old when treatment was begun.*

(*a*) *Caries was very active in most of the teeth and, in the section illustrated, the complete absence of secondary dentine suggests defective defensive mechanism.*

(*b*) *The healing or arresting process was in progress and the section of the extracted tooth shows the associated barrier of well-calcified secondary dentine.*

(*c*) *Section of tooth extracted from another child after three years' cod-liver oil therapy. The previously soft carious tissue had then become hard and the section demonstrates the defensive process in the form of well-calcified secondary dentine.*

increase the vitamin D and calcium intake, the latter preferably in the form of milk; this is especially important for pregnant women, infants and children[1].

When we consider how vitamin D produces these effects we are in an atmosphere of pure surmise. The quantities necessary are amazingly small. For instance, it is probable that 500 to 1,000 international units of vitamin D given daily from birth to adolescence would produce perfectly formed bones and teeth if the food was otherwise reasonably good. Now there are 40,000 international units in 1 mg. of calciferol (vitamin D_2), so the necessary daily amount would be $\frac{1}{80}$ to $\frac{1}{40}$ mg., say about 8 mg. a year for the first 15 years, and perhaps a total of $\frac{1}{2}$ gram for the normal life-span of three-score years and ten. In an experiment on a dog the effect of 7,000 international units of vitamin D_2 ($\frac{1}{6}$ mg.) taken over a period of 7 days was to convert a daily negative calcium balance into a markedly positive one. We are obviously at the level of powerful enzymic action. If, as seems probable, calcium and phosphorus metabolism involves the formation of calcium hexosephosphate, it may be surmised that vitamin D has some controlling influence over phosphatase activity in relation to calcification.

The functions of vitamin D in the body are best understood by a study of the conditions resulting from its absence or deficiency, especially during infancy and childhood. With such a

[1]It is essential that vitamin D preparations, and especially cod-liver oil, should be carefully stored. A fact which is not always appreciated is that they tend to lose their potency under certain conditions, including exposure to light and air.

deficiency the muscles are flabby, the growing bones are relatively soft and bent (figure 1), and the teeth forming at the time are badly calcified and liable to decay (figure 2 (*b*, *c*, and *d*)). (In an examination of 1,300 6-year-old school children in 1929, none was found to have a full set of perfectly formed teeth, and only 4·7 per cent. were free from caries.) This deficiency in early life is reflected in the bent legs and stunted growth of many adults and in the toothless mouths of thousands of middle-aged people. A more serious, but less obvious, result is the badly formed pelvic bones (contracted pelvis) which later so often interfere with normal childbirth. In some large cities where rickets used to be very prevalent, the Caesarean operation is common and mishaps to mother and infant due to contracted pelvis are still abnormally high. A deficiency of vitamin D in adult life can also produce serious results, especially during pregnancy, and these become more prominent in post-war periods and during times of great food restriction.

There is one great difference between calcification processes in bones and teeth which needs emphasis. During the period of growth there is a constant absorption and redeposition of bone tissues, whereas once a tooth is formed it cannot be radically changed. If an infant or child develops bone deformity owing to a deficiency of vitamin D, the old operation of osteotomy, which consists of breaking and resetting the bones, is no longer necessary provided the child is growing, since the condition can be remedied by adding the vitamin to a good general diet, though it may take several years of this therapy to straighten the legs. If, on the other hand, dental structure is bad at any period of development, the part formed at that time will remain bad, although it has been shown in dogs that the addition of vitamin D or cod-liver oil to the diet will cause any later-formed tissue to be well calcified. This is illustrated by figure 6.

Examination of large numbers of deciduous and permanent human teeth between the years 1921 and 1934 showed that, by whatever method they were examined—*in situ*, macroscopically after shedding or extraction, or histologically—not more than 10 per cent. of the deciduous and 7 per cent. of the permanent teeth were of really good structure according to the standards used. All the rest showed some degree of defect, as illustrated in figures 2 and 7. Since the structure of our teeth is influenced by fat-soluble vitamins, especially vitamin D, we cannot afford to allow such vitamins to be deficient at any time during the period of dental development.

While it would be wrong to give the impression that if teeth were perfectly formed all caries would cease, it can be stated quite definitely that there is a real relationship between tooth structure and susceptibility to caries, poorly formed teeth being much more likely to suffer decay than well-formed teeth. For instance, in the collections of children's teeth referred to above it was found that there was no caries in 78 per cent. of the well-calcified teeth, whereas only 6 per cent. of those with very poor structure were free from decay. Conversely, caries was extensive in only 7·5 per cent. of the well-formed as compared with 74 per cent. of the very badly formed teeth.

When a tooth is attacked by caries, it tries to defend itself against the invading micro-organisms if conditions are favourable. Here again vitamin D is called for, and if sufficient be provided, together with plenty of calcium and phosphorus in the form of milk, the attacked tooth may build up a barrier of new dentine (secondary dentine) as a defence; the progress of the disease may thus be arrested and the tooth may become 'healed.' An example of 'healed' caries can be seen in figure 8 (*c*). Thus a sufficiency of vitamin D will not only act as a main factor in procuring perfectly formed teeth, but will also help teeth attacked by caries to defend themselves. Again, how this is done remains to be discovered.

Although it has been shown above that vitamin D is not the only factor to be considered in dental and bone structure, it is probably the main factor and is certainly the one most likely to be deficient in the diet of people in temperate zones.

Recent work on dogs has shown that vitamin A, as well as vitamin D, plays a part in bone and tooth structure, but it has quite a different function from that of vitamin D. As regards bones, whereas the effect of vitamin D is to harden them, vitamin A regulates the activity of bone-forming cells; in its absence they become too active, and overgrown bones are produced. In the case of the teeth the effects of a deficiency of vitamin A are less obvious, but owing to overgrowth of the cementum the roots tend to become stunted. There are undoubtedly nutritional factors other than vitamins D and A, calcium, phosphorus, and phytic acid concerned in the formation of bones and teeth and in the protection of the teeth against decay, but, except as regards this latter instance, the back of the problem has probably been broken.

The war has caused a greatly increased interest

in human nutrition, and many nutritional surveys are being made. The general result has not shaken the view that vitamin D is still the greatest single deficiency in the British diet. In the period between the last war and this one there was a definite improvement in the growing population, especially in industrial areas, but there is reason to believe that during the present war rickets is again on the increase. The Government has recently, however, taken steps to remedy this by supplying more cheap or free milk to the young, by adding calcium carbonate to the national flour to antagonize the additional phytic acid it contains, by adding vitamins D and A to all margarine, and by making cod-liver oil and other vitamin D preparations easily available. With our present knowledge of nutrition, and especially of the factors controlling bone and tooth formation, it ought to be possible to ensure for coming generations good hard bones and white, shiny teeth comparatively free from decay and regularly arranged in well-developed jaws.

Book reviews

THE PHILOSOPHY OF A SCIENTIST

Physics and Philosophy, *by Sir James Jeans, O.M. Pp. vii + 222. Cambridge University Press, London.* 1942. 8*s.* 6*d. net.*

Some of the most original and valuable contributions made to philosophy in this century have been due to men who began life as mathematicians or mathematical physicists—A. N. Whitehead, Bertrand Russell, J. H. Jeans, A. S. Eddington, and H. Jeffreys, all of whom were products of the Cambridge mathematical tripos; and this is natural enough: for it is no longer possible to philosophize about space, time, and matter without understanding relativity and quantum-mechanics. The prospect that in the future the typical occupant of a university chair of philosophy will be an ex-mathematician is brought still nearer by this profoundly interesting little volume.

Sir James considers, in the light of modern physical concepts, the rival doctrines of materialism and subjective idealism, and shows that Berkeley's argument, though invalid for the purpose for which he intended it, can be used to prove that mind and matter have something in common. He then compares the duality of mind and matter with the duality of waves and particles in quantum-mechanics; as he points out, the ingredients of the particle-picture are particles existing in physical space, while the ingredients of the wave-picture, which are waves of knowledge, are mental constructs existing in conceptual space: the ingredients of the particle-picture are material, those of the wave-picture mental. Since we find that we can best understand the course of events in terms of waves of knowledge, there is a certain presumption that reality and knowledge are similar in their natures or, in other words, that reality is wholly mental. In any case, the two members of the new dualism—waves and particles—are not antagonistic or mutually exclusive as mind and matter were: they fit harmoniously into a unity, the waves controlling the particles: in the old terminology, the mental controls the material.

The discussion of the consequences of Heisenberg's uncertainty-principle may also be specially commended.

E.T.W.

SPECTROSCOPY AND COMBUSTION

Spectroscopy and Combustion Theory, *by A. G. Gaydon. Pp. x + 191. Chapman & Hall Limited, London.* 1942. 17*s.* 6*d. net.*

In the analysis and systematization of band-spectra on the basis of the quantum theory, many band systems produced in flames were assigned to emitting radicals such as CH, NH, OH, C_2, and CN, whose existence, though long suspected, had not previously been satisfactorily established, and the electronic, vibrational and rotational states of these emitters in flames were completely determined. Later studies have led to an understanding of the presence and roles of these intermediate products in combustion processes and have yielded much new information on flame reactions.

Dr. Gaydon's book deals entirely with these spectroscopic investigations. It opens with an elementary account of the theory of molecular spectra and of the conditions under which band systems appear in emission, and leads, through brief descriptions of several types of flame spectra, to applications of spectroscopy to derivations of lifetimes of activated molecules and dissociation energies, the after-burning of carbon monoxide and the kinetics of the combustion process.

A 20 pp. appendix giving numerical data and other information on molecular spectra and energy levels in flames, two plates of excellently reproduced flame spectrograms, and an adequate index, add considerably to the usefulness of a monograph which is unreservedly recommended to all who are interested in or engaged on combustion problems.

W.J.

A CONCISE HANDBOOK TO MILITARY 'GASES'

War Gases: their Identification and Decontamination, *by Morris B. Jacobs. Pp.* 180. *Interscience Publishers Inc., New York; Imperia Book Company Limited, London.* 1942. $3 *net.*

This is an excellent compendium for gas identification officers, war gas chemists, decontamination officers, public health officers, and all others interested in chemical warfare. It is not so detailed or comprehensive as previous books on the subject, such as Prentiss and Sartori, but it presents in simple, concise, and systematic manner the essential information regarding the

identification of the various types of toxic gases and the methods for decontaminating materials of all kinds polluted thereby. Its exact contents are displayed in the chapter headings: Classification of the Chemical Agents; Physical Characteristics and Physiological Response of the War Gases; Effect of War Gases on Materials, Water, an dFood: Sampling; Scheme of Analysis; Detection and Determination of Arsenic; Confirmatory Tests; Decontamination.

The main facts and procedures have been collected from British A.R.P. publications and other official sources. The volume contains little that is new, but it is accurate and easy to read and to understand. A great deal of the more important material is admirably summarized in tabular form, but it is unfortunate that Table III in the Appendix (Order of Toxicity of the War Gases) conflicts, in many cases, with the data in preceding tables and omits phosgene altogether.

JAMES KENDALL

A SYNTHESIS OF MORPHOLOGY AND BIOCHEMISTRY

Biochemistry and Morphogenesis, *by Joseph Needham. Pp. xvi + 787. Cambridge University Press, London.* 1942. *52s. 6d. net.*

There are signs that, after the age of specialization which was the intellectual accompaniment of the later developments of *laissez faire*, we are now returning to the broad synthetic sweep which has been the usual aim of civilized man. Dr Needham's monumental work is one of the signs of this return. In it he takes the data of two biological disciplines which up till quite recently have been pursued in isolation and succeeds to a remarkable degree in synthesizing them in a mutually illuminating fusion. Both are active growing points of biological science. Biochemistry is rapidly unravelling the chemical processes underlying vital activity: experimental embryology or *Entwicklungsmechanik* is formulating the empirical principles of animal and plant development. The two are on different planes of study. Needham has succeeded in building staircases connecting the two sets of levels.

In a brief review, all that can be done is to pick out a few high lights. Perhaps the most spectacular is the way in which the cancer problem is illuminated. In the first place, the chief carcinogenic substances are closely related chemically to the substance which acts as evocator in the vertebrate organizer (as well as to the sex hormones). Secondly, the evocator exists in a masked form in all parts of the embryo, probably in combination with a specific protein, and its activity in the organizer region is due to this combination being here broken, through some peculiarity of metabolism. A formal explanation of cancer, superseding the idea of 'embryonic rests' and furnishing a more satisfactory alternative to the virus theory, is provided by the idea that a masked carcinogen is similarly liberated under certain abnormal conditions of metabolism. Much work remains to be done, but it is clear that a new and hopeful approach is provided.

Similarly the biochemical facts, largely elicited by the Needham school, as to the nature and mode of working of the evocator substance, and its co-operation with the chemical 'competence' of the reacting tissue and with the individuation field of the whole embryo, are throwing light on numerous problems of normal development and regeneration, and on the mode of action of hormones and of genes.

The gradual clarification of the idea of the developmental field, an empirical notion entirely derived from the facts of *Entwicklungsmechanik*, is in its turn illuminating the chemical study of growth, while from the opposite side our knowledge of liquid crystals is helping us to understand and to define the properties of developmental fields.

It would be possible to continue indefinitely. Here we can only say that all serious students of biology, whether biochemist, embryologist, physiologist, geneticist, cancer worker, growth specialist, or general evolutionist, will find valuable new light on their old problems in Needham's pages. The book is exhaustive and heavily documented, and contains numerous fascinating excursions into collateral issues. The present reviewer has only one regret—that Needham has deliberately excluded the field of invertebrate regeneration from his survey.

Biochemistry and Morphogenesis is more than a successor to Needham's previous great work *Chemical Embryology;* for while that was essentially a survey, this is essentially a creative synthesis. It is one of the most important contributions to biology made in the present century, and will secure for its author a permanent place in the history of science. JULIAN HUXLEY

ABSORPTION SPECTRA IN BIOCHEMISTRY

The Application of Absorption Spectra to the Study of Vitamins, Hormones, and Coenzymes, ***by R. A. Morton. Pp. 226. Adam Hilger Limited, London. Second edition,*** **1942. 28*s. net.***

In the application of spectroscopy to biochemical problems, far the most important advance was the development of the ultra-violet spectroscope and spectrophotometer. Among compounds of biological interest there are many more uncoloured than coloured, but a high proportion of those that are completely transparent to visual light have been found to show characteristic absorption spectra in the ultra-violet region. Measurement of the wavelength and intensity of this 'invisible colour' is now a commonplace operation, even in many routine industrial laboratories, serving as a highly accurate analytical method, and has played at least as great a part as visual spectroscopy in helping to establish the constitution and investigate the metabolic roles of many of the substances discussed in Dr Morton's admirable monograph.

This edition is nearly four times as long as the first. It is impossible here even to begin to detail the many advances that have been recorded during the intervening seven years, but it is symptomatic that two of the chapters in the new edition, those on 'Vitamin E and Anti-oxidants' and 'Vitamin K,' are represented in the original edition by just over two pages about vitamin E; the existence of vitamin K was hardly recognized in 1935. Other advances of which Dr Morton takes cognizance are our knowledge of the interrelationship between certain water-soluble vitamins and enzyme systems, and the clear establishment of a structural connection between the steroid hormones, the anti-rachitic vitamins, and the active substances of the adrenal cortex.

In order to make clear the part played by spectroscopic technique in helping to establish the progress recorded by Dr Morton, he has had to discuss in considerable detail the chemistry of all the fat-soluble vitamins (A, D, E, and K), of many water-soluble vitamins [C, B_1 (aneurine), riboflavin, nicotinic acid, pyridoxin (B_6)], as well as some of the borderline cases such as vitamins P and H, and has also devoted a chapter to purine and pyrimidine derivatives and a few

pages to the spectroscopy of some amino-acids. The tenth and last chapter, on 'Enzymes and Coenzymes,' gives a concise but extremely useful summary of our knowledge of several of the most important cellular enzyme systems. The book thoroughly deserves a wide circulation amongst all who are concerned with the chemical aspects of fundamental cellular processes in animal and plant organisms.

A. L. BACHARACH

A QUANTITATIVE STUDY OF PLANT REPRODUCTIVITY

The Reproductive Capacity of Plants, *by E. J. Salisbury. Pp. xi* + 244, *with 7 plates and* 35 *text figures. G. Bell & Sons Limited, London.* 1942. 30*s. net.*

This remarkable book is the first extensive quantitative account of the reproductive capacity of flowering plants. Reproductive capacity is determined by seed output and viability and, as both are highly variable, many counts are necessary. The labour of gathering the data for a large number of British plants must have been heroic. The main object of the book is to provide a foundation for conclusions as to the effect of reproductive capacity on survival and dispersal, and this theme is treated from various angles. There are accounts of special systematic and ecological groups, such as the gentians and St. John's worts, and the saprophytes and parasites. The relation of seed size to type of community, open or closed, is discussed. As between different species of the same genus, a case is made for the view that comparative rarity goes along with lower reproductive capacity. A final chapter on vegetative propagation is of special interest and includes several valuable figures. Here Professor Salisbury's happy gift of picking significant and striking facts from his extensive observations in field and garden is notably evident. The data might have been presented in a more condensed form without impairing the value of an important work.

M. SKENE

THE STUDY OF SOCIETY

Social Structure, *by H. A. Mess. Pp.* 130. *George Allen & Unwin Limited, London.* 1941. 6*s. net.*

All books popularizing social study are welcome today, when clearly we must obtain an increased understanding of those processes which have brought our civilization into such violent disarray. There has been a flow of books about the social sciences, without (as yet) one really complete and coherent analysis either of the latest knowledge, or of the best available methods for its scientific study. In the meanwhile, Dr Mess has contributed another to the growing list of useful little volumes.

Social Structure is well written, interestingly arranged, stimulating. Its main weakness is one common to most of these sociological primers: a lack of factual illustration based on objective study. Dr Mess relies on generalizations which are often subjective and unsupported by reliable evidence. He frankly finds himself faced with terminological difficulties of verbal definition; until we have a much closer analysis of what actually happens in human affairs we are bound to use academically imposed categories and classifications. He himself gets caught up in these—for instance when discussing 'Community' (p. 78) or distinguishing between intellectual aspects and emotional associations (p. 119). The result is sometimes very confusing.

T.H.

SHORTER NOTICES

Hydrogen Ions, *by Hubert T. S. Britton. 2 vols., pp. xix* + 420 *and xix* + 443. *Chapman & Hall Limited, London. Third edition,* 1942. 36*s. net each volume.*

This well-known book, first published in 1929, rapidly established itself as the standard work on the subject, and a second edition was called for in 1932. For the present edition, published in two volumes, the author has revised the whole text and made substantial additions which will greatly increase its usefulness. We are particularly glad to note the inclusion of a chapter on Redox potentials, the symbol rH, and the use of Redox indicators. The importance of pH control in a wide variety of applied chemical fields is very clearly discussed, as is also relevant modern work in inorganic and analytical chemistry. Professor Britton has written a book of distinction.

The Structure of Steel simply Explained, *by E. Gregory and E. N. Simons. Pp. xv* + 140. *Blackie & Son Limited, London. Second edition,* 1942. 5*s. net.*

An interesting and plainly written little book which describes the structure of steel with a minimum of technical phraseology. The general scientific reader who wants to know something about those numerous and diverse metallic substances subsumed under the single title of 'steel' could not do better than follow the lucid story here told by Dr Gregory and Mr Simons.

War against Disease, *by Milton Silverman. Pp.* 284. *Michael Joseph Limited, London.* 1942. 12*s.* 6*d. net.*

Popular scientific books often fall between two stools—if they are popular they are frequently inaccurate scientifically, while scientific precision is liable to limit their popular appeal. Mr Silverman's book—the sub-title of which is 'Miracles of Modern Medicine'—suffers from neither defect. It tells in a vivid and dramatic manner of the discovery of quinine, cocaine, aspirin, the vitamins, sulphanilamide, etc., and the author has obviously been at great pains to verify his facts. The style of the book has necessitated the introduction of imaginary conversations, but this is quite a legitimate device. We recommend the book to scientists and laymen alike; it should certainly be in every public library.

Twins and Super-twins, *by H. H. Newman. Pp.* 164, *with* 19 *illustrations. Hutchinson & Company (Publishers) Limited, London.* 1942. 10*s.* 6*d. net.*

Professor Newman, who for over a quarter of a century has made a special study of multiple human births, here attempts to give systematic and reliable answers to such questions as 'What causes twins?' 'Are twins likely to be sterile?' 'How many kinds of twins, triplets, etc., are there?' 'Are twins desirable?' He has collected a great deal of information on the subject and his book is worth reading.

Mathematics: its Magic and Mastery, *by Aaron Bakst. Pp. xiv* + 790. *Chapman & Hall Limited, London.* 1941. 21*s. net.*

This book, first published in the United States, compares not unfavourably with *Mathematics for the Million*. It is a skilful effort to make the fundamentals of mathematics interesting and even amusing to the general reader, by presenting the science in the light of its versatility in the various fields of human endeavour. With the proviso that the reader must keep his wits constantly on the alert, the effort must be regarded as very successful. An excellent gift-book for intelligent young people.

Notes on contributors

SIR LAWRENCE BRAGG,
O.B.E., M.C., M.A., D.Sc., F.R.S.

Son of the late Sir William Bragg, O.M., K.B.E., F.R.S., he was born at Adelaide, South Australia, in 1890, and was educated at St Peter's College, Adelaide, the University of Adelaide, and the University of Cambridge. As Fellow and Lecturer in Natural Sciences at Trinity College, Cambridge, he carried out (in collaboration with his father) work on X-rays and crystal structure which was awarded the Nobel Prize for Physics in 1915. During the war of 1914–18 he was Technical Adviser on Sound Ranging to the Map Section, G.H.Q., and from 1919–37 was Langworthy Professor of Physics in the University of Manchester. He was afterwards appointed Director of the National Physical Laboratory, and in 1938 succeeded the late Lord Rutherford as Cavendish Professor of Experimental Physics in the University of Cambridge. He strongly opposes the view that industrial research has lesser claims to be called scientific, and is in some way of a lower order, than university research. He also holds that it is the duty of a scientist not only to do research but to put it into a form in which it can be appreciated by other busy people. He takes a great interest in science teaching and is at present engaged in a campaign to make it less specialized at both schools and universities.

His main outside interests are in reading the best modern books as they come out, and in sketching. He and his wife have visited practically every country in Europe, where they have made personal friends of many scientists. He has also paid three extended visits to America as a university teacher, and has always enjoyed his time there.

COLONEL SIR HENRY LYONS,
Hon. D.Sc. (Oxon.), Hon. Sc.D. (Dublin), F.R.S.

The son of General T. C. Lyons, C.B. (Governor of Bermuda, 1892–96), he was born in 1864 and was educated at Wellington College and the Royal Military Academy. Commissioned in the Royal Engineers in 1884, he subsequently served at Gibraltar and in Egypt. He was Director-General of the Geological Survey, Egypt, from 1896 to 1898, and of the Survey Department of that country from 1898 to 1909. After his retirement from the Egyptian Service, he became Lecturer in Geology at the University of Glasgow and was subsequently appointed to the staff of the Science Museum, of which he was made Director in 1920. He was Foreign Secretary of the Royal Society in 1928–29 and Treasurer from 1929 to 1939.

A. D. IMMS,
M.A., D.Sc., F.R.S.,

Was born at Moseley, Birmingham, in 1880. Educated at the University of Birmingham and at Christ's College, Cambridge, he is now a Fellow of Downing College, Cambridge. In 1907 he became the first professor of zoology in Allahabad University and, later, Forest Zoologist to the Government of India. He subsequently accepted the post of Reader in Agricultural Entomology at the University of Manchester, and in 1918 was appointed Chief Entomologist at the Rothamsted Experimental Station. In 1931 he returned to Cambridge to take up the new post of Reader in Entomology founded under a Rockefeller benefaction. His entomological studies have taken him to many parts of India, to Ceylon, Canada, the United States, and the Hawaiian Islands, and to many European countries. He has written several books and papers on entomology, and is a past president of the Royal Entomological Society and of the Association of Applied Biologists. He is fond of motoring and gardening and is attracted to the Western Highlands of Scotland.

J. N. ALDINGTON,
B.Sc., A.I.C., F.Inst.P.,

Was born in 1905, and was educated at the Balshaws Grammar School, Leyland; the Harris Institute, Preston; and the Technical College, Blackburn. He has been with Messrs Siemens Electric Lamps and Supplies Limited since 1923, and is now Assistant Works Manager of the firm, with responsibility for technical development and control. He is the author of various papers and articles dealing particularly with developments in electric discharge lamps, and in 1942 was awarded the Leon Gaster Memorial Premium for a thesis on fluorescent light sources and their applications. He is a keen amateur gardener, and before the war played golf.

A. R. TODD,
D.Sc., F.I.C., F.R.S.,

Was born at Glasgow in 1907 and was educated at Allan Glen's School and the University of Glasgow. He continued his studies at the Universities of Frankfurt a/M. and Oxford, and in 1935–36 was Beit Memorial Research Fellow at the University of Edinburgh. He later joined the staff of the Lister Institute of Preventive Medicine, London, and after holding the posts of Reader in Biochemistry in the University of London and Visiting Lecturer in the California Institute of Technology was appointed Professor of Chemistry and Director of Chemical Laboratories in the University of Manchester (1938). He has always been fascinated by the biological side of organic chemistry, to which he has made numerous and important original contributions. His favourite recreations are lawn tennis and travel.

LADY MELLANBY,
Hon. D.Sc. (Sheffield and Liverpool),

Became interested in science when a student at Girton College, Cambridge. After taking both parts of the Natural Sciences Tripos, she became a research student at Bedford College, London, and later a lecturer on physiology in that college. In 1914 she married Dr E. Mellanby (now Sir Edward Mellanby, K.C.B., F.R.C.P., F.R.S.). In 1916, when working with her husband on the causation of rickets—work which led to the discovery of the calcifying or antirachitic vitamin (D)—she noticed the effect of this vitamin in promoting the formation of good teeth, and from that time made dental science her own particular field. Most of the fundamental observations described in relation to teeth in her article in the present issue were made by herself, and she has published many papers on different aspects of her work, including three reports in the Medical Research Council's Special Reports Series. As the result of an accident in her Cambridge days, she is unable to take any active part in sport, but finds recreation chiefly in her work and in travelling.

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